JOURNAL OF

GENERAL CHEMISTRY

OF THE USSR

(ZHURNAL OBSHCHEI KHIMII)

IN ENGLISH TRANSLATION

$$\frac{c}{b}$$

CONTENTS

CONTENTS (continued)

CONTENTS (continued)

CONTENTS (continued)

CONTENTS (continued)

VLADIMIR YAKOVLEVICH KURBATOV

(1878 - 1957)

K. P. Mishchenko and V. V. Razumovskii

Vladimir Yakovlevich Kurbatov passed away on February 12, 1957, at the age of 80. V. Ya. Kurbatov belonged to the class of encyclopedic scientists,in that his scientific studies embraced varied fields in both chemistry and chemical technology.

V. Ya. completed his work in the Natural Sciences Division of the Faculty of Physical Mathematics at St. Petersburg University in 1900. In October 1900, a vacancy for the position of laboratory worker (at the time they were called assistants) arose in the Chemistry Department of St. Petersburg University, and V. Ya. was invited by D. P. Konovalov [1] to take the position. In the university laboratory V. Ya. did experimental work on the nature of liquids, and at the same time, at the suggestion of D. I. Mendeleev, he made a study of thio salts.

In 1905 V. Ya. was sent by St. Petersburg University to the laboratory of Henri Le Chatelier in Paris to learn about the latest advances in methods for studying metal alloys. The eminent French scientist gave the young Russian chemist the problem of finding techniques for distinguishing the different components of hardened steel. It proved that V. Ya. was able to solve this problem in a short time, capitalizing on his profound knowledge of the nature of liquids. For this purpose he developed the "Kurbatov reagents" or etching solutions, which·are used in practice at the present time to bring out the microstructure of steel [2].

V. Ya. began his career as a teacher in 1905, teaching a course in general chemistry in the Agronomy Section of St. Petersburg University. On May 17, 1907 V. Ya. was competitively selected to teach physical chemistry at the St. Petersburg Technological Institute, where he founded the Department of Physical Chemistry [3], which he headed for 50 years. He also founded the Department of Colloid Chemistry at the same Institute. At the same time, V. Ya. served as principal of the Science Education section, annually taking part in various commissions of the Institute. In 1908 V. Ya. took part in organizing the Chemical Faculty of the Women's Polytechnical Institute. Together with A. A. Baikov, he gave invaluable help to P. N. Ariyan, the founder of this school of higher technical learning for women, the first of its kind in the world, in setting up the study plan and the study programs. Fron 1908 to 1923 V. Ya. taught courses in both physical and colloid chemistry to students destined to be the first Russian women engineers [4]. In 1915 V. Ya. was appointed director of the Laboratory for Testing Materials in the Ministry of Agriculture. During the First World War he served as consultant on the design and construction of chemical plants, operating in the defense of the country.

After the Great October Socialist Revolution V. Ya. immediately took part in setting up the Soviet government. As early as 1917 V. Ya. was appointed scientific consultant to the People's Commissariat of Education. He took an active part in the erection of Soviet higher schools, and at the same time he did yeoman work in the preservation of art relics and antiques. In 1918 V. Ya. was one of the organizers of the Chemical Division of the Higher Soviet National Economy. He was of great help in putting into operation in Petrograd the first plant for the extraction of radium. In 1919 V. Ya. was appointed a member of the Soviet National Economy of Siberia. In 1923 he was consultant to the Agricultural Exhibition in Moscow. V. Ya. Kurbatov was one of the initiators and participants in supplying to the government the reports of trained chemists on the chemization of the national economy.

In 1928 the Council of People's Commissars of the USSR formed the Committee on the Chemization of the National Economy, and V. Ya. was appointed a member of this committee. In the same year he was sent to

VLADIMIR YAKOVLEVICH KURBATOV

(1878 - 1957)

France, where he delivered a paper entitled "The Structure of Liquids" at the First International Convention of Physical Chemists.

During the years of industrialization, V. Ya. turned his creative talents to the development of chemical expansion and the organization of new chemical industries. He helped in solving various problems of a chemical and technical nature for the Research Institute of Plastics, Central Laboratory of the "Red Triangle" Rubber Factory, All-Union Aluminum-Magnesium Research Institute, Central Battery Laboratory, All-Union Research Institute on Fats, Nevsk Stearin Plant, shoe factory "Skorokhod", and other enterprises.

During 1931-1939 V. Ya. fulfilled the honorary and functional duties of a deputy of the Leningrad City Council of Deputies working at the XIII and XIV Meetings.

During the years of the Great Fatherland War in 1941-1945 the tirelessly conducted special scientific studies, acted as consultant to a number of plants and factories, operating in the defense of the Country, and suggested a method for the underground storage of world art relics.

Developing the atomistic theory during 1906-1907, Kurbatov extended it to the structure of the cosmos and 23 years before the discoveries of the American astronomer Hubble predicted the existence of supergalactic systems in the universe. Here Kurbatov wrote "but there is no basis to believe that it is not possible for entities, composed of star systems, to exist, the same as the latter are composed of solar systems" [42, 46]. * Proceeding from the theory of Mendeleev regarding the complex structure and divisibility of the atom, V. Ya. arrived at the following conclusion in 1907 regarding the complex structure and divisibility of the atom: "In exactly the same manner it is impossible to think that electrons are the limit of divisibility. Once it is assumed that the universe is infinite, then electrons also are divisible" [42, 46]. During this same time Kurbatov made the statement that "some electrons of the atom cleave easily, and, as a result of them, electrostatic (electrolytic) bonds are formed between the atoms". In this connection the "number of such electrons corresponds to the designation of the group in the Mendeleev law [to the extent that it is not masked by the ability of the atom to add such electrons (Groups 4, 5, 6 and 7)]" [46].

The physical meaning of this tenet was later enunciated by the theory proposed by N. Bohr for the structure of the atom. According to Kurbatov, "the alkali metals and silver have one electrolytic valence, the second group has 2, the third group has 3, and the fourth group has 2 in the compounds $SnCl_2$ and $PbCl_2$ . . . As regards the negative type of valence, i.e., the ability to add electrons, then, undoubtedly, it is equal to one in the seventh group, and possibly is equal to two in the sixth group, since there are indications that sulfur compounds show electrolytic conductivity" [46].

In the opinion of V. Ya., the number of electrovalences possessed by atoms of chemical elements varies with the groups in the Mendeleev periodic system. He came to the conclusion that two types of chemical bonds exist. In chemical compounds—electrolytes—the atoms are bound to each other by the attraction of opposite electric charges. He emphasized that "it is necessary to assume the existence of special bonds in order to explain compounds that do not undergo electrolysis, for example, $SnCl_4$, CH_4, etc." [46].

These ideas of Kurbatov preceded in part some of the tenets of the electron theories as proposed by Kossel (1916) and by Lewis (1916) for the chemical bond and the structure of molecules.

Kurbatov believed that "there exists a series of transitions between compounds capable of becoming electrolytes, and compounds not capable of being such" [46].

As a result, according to the concepts of V. Ya., between chemical compounds with an ionic (electrostatic) bond and chemical compounds (nonelectrolytes) with an atomic bond there exist all degrees of transition, which fix the unity of these opposite forms of compounds. The studies of V. Ya. contributed substantially to the development of the periodic law [5].

The principal physicochemical studies of V. Ya. were made in the field of the structure of liquids, which studies he conducted systematically and in a well-planned manner for a period of sixty years. In 1898, while still

---

* References to the works of V. Ya. Kurbatov are given in the section "Bibliography of Principal Scientific Papers".

a student, he began to study, in the laboratory of D. P. Konovalov, the latent heat of vaporization of aniline hydrochloride and its dissociation when vaporized. In 1902 V. Ya. made the more difficult measurements of the latent heat of vaporization of mercury. His experiments on the latent heats of vaporization of liquids disclosed exceptions to the Trouton rule. The results of these studies were reported by him in 1902 at the International Convention of Naturalists in Helsingfors. These studies are classic and are still important at the present time. In 1904 V. Ya. finished his study of the heat properties of aniline and their dependence on the temperature, which led to establishing the presence of a minimum heat capacity for aniline, and this refuted the universality of the Schiff rule regarding a linear relationship. The first observations caused him to think about the nature of the association of liquids, i.e. the nature of intermolecular cohesion.

During the period from 1903 to 1945, V. Ya. gradually accumulated a vast amount of experimental data: he investigated the properties of more than 400 liquids. As early as 1907 V. Ya., in examining the experimental material at his disposal, arrived at the opinion that crystalline properties are manifested in the liquid state [46]. Later studies of V. Ya. confirmed the validity of this opinion. It proved that in his opinions regarding the nature and structure of liquids, V. Ya. preceded by some 10 to 20 years the tenets and concepts held by all at the present time.

The experiments made by V. Ya. on determining the heat capacity of superheated vapors for 80 compounds are the first and among the very few experiments reported in the literature. Using as a base the obtained experimental data, he created in 1916 a theory for the structure of liquids, according to which the particles of liquids are not only attracted to each other as a whole, but to a greater or less degree also exchange ions, atoms, and radicals.

The basic idea of V. Ya. Kurbatov's theory reduces to the statement that "a molecule of water is equal to its given mass, independent of whether we are dealing with a drop or with the ocean" [78]. This thought, expressed by V. Ya. in 1916, was repeated in peculiar form some twenty years later by Langmuir at the International Physical-Chemical Congress in Edinburgh (1936) without reference to Kurbatov.

The theory of V. Ya. exposes the dynamic nature of liquids, recognizing the existence of a continuous exchange between the component parts of the molecules of liquids. This theory is in complete accord with contemporary viewpoints, and preceded the opinions regarding the nature of liquids by many years. The entire community of investigations made by V. Ya., devoted to studying the structure and properties of liquids, represents a unified and purposeful task of capital proportions. Based on his investigations, V. Ya. set up a number of approximate rules for the heat properties of liquids.

V. Ya. made a major contribution to the theory of the formation of crystals, gels, and colloids. As early as 1917 he stated that ionic exchange takes place in the vapors of compounds whose molecules have an ionic bond; in liquids exchange takes place between the component parts of their molecules, in particular, electron exchange; in the case of ionic crystals it is electron exchange that is realized. Proceeding from these tenets, he continued on to make further discoveries regarding the processes of crystal formation. It was stated by V. Ya., that "the strength of crystals (hardness, melting point) increases in going to the ions with higher valences, and is especially sharp in the transition from monovalent to divalent ions. The rate of crystallization decreases with increase in the valence of the ions, and is especially sharp in going from divalent to trivalent ions" [86, 87].

These rules, established by V. Ya. in 1924, were later confirmed by numerous experiments and observations, made both in the laboratory and in production practice. The Kurbatov rule regarding the relationship between the strength of crystals and the valence of their ions received experimental proof in 1927 in the investigations of the German scientist Goldschmidt.

The process of crystal formation was regarded dialectically by V. Ya. as a unity of opposite processes of formation and decomposition. He rejected the possibility of forming an ideal crystal, proving his position by the unity of the opposite influences exerted by the centers of crystallization and the mother medium. If the centers of crystallization cause a mutual coordination of the ions, then on the other hand, the mother medium (liquor, melts) and impurities (foreign ions) upset this coordination. According to his theory, the principal sources of crystallization centers are, as a rule, those created by a coupling of the ions of the principal substance with the ions of the impurities, giving the most rapid crystallization with the highest strength for the crystal. Usually this is a combination of divalent ions, appearing as impurities and forming the first centers of

crystallization. Optimum crystallization, remarked Kurbatov in 1920, lies in the divalent ions, and they are not centers for the crystallization of gels of multivalent inorganic and organic ions (compounds of aluminum, silicon, carbon . . .). The salts of monovalent ions sharply lower (when compared with divalent ions) both the strength of the crystals and the temperature of crystallization, but they also accelerate crystallization, not permitting substantial supercooling. The salts of tri- and tetravalent ions permit substantial supercooling, and they crystallize slowly, but the crystals are very strong. Decreasing the degree of ionization shown by salts results in decreasing both the strength of their crystals and the temperature of their crystallization.

According to the theory of Kurbatov, gels and colloids, whose basic external characteristic is the absence of crystallization, can exist only if their skeleton contains crystallization centers that develop quite slowly. It is possible for the crystallization centers to have the composition of the principal substance present in the gel or colloid, and it is also possible for them to have a different composition, especially that of divalent ions, corresponding to the optimum crystallization. According to Kurbatov, the process for the formation of gels consists in a successive chemical polycondensation of the molecule with the ions having a high valence, accompanied by an entrapment of the solvent molecule, and terminating in the formation of a gigantic molecule.

The concepts developed by V. Ya. in the period from 1917 to 1924 regarding the universal nature of the amphoteric state show that all substances in sufficiently acid medium are cations, in sufficiently alkaline medium they are anions, and in the transition state they are amphions. The tenets of V. Ya. regarding the universal nature of the amphoteric state for substances received expansion in the most recent theories regarding acids and bases [6]. According to the theory of Kurbatov, amphions, having a balanced charge due to the neutralization of opposite charges and the separation of water, form one common polyamphion, $nH + (HAlO_2)^-OH \rightleftharpoons (HAlO_2)_n + nHOH$.

Because of heat motion in different portions of the polyamphion, it is impossible to have a complete balancing of the charge. For this reason it is possible to have in some portions of the amphion the addition of water and a rupture of the bonds between amphions, while in other portions, quite close to the balanced charge state, it is possible to have the separation of water and a strengthening of the bonds between amphions.

Kurbatov regarded protein macromolecules in the neutral state as being polyamphions of amino acids. If, at the time, the concept of V. Ya. that the protein macromolecule was a polyamphion met with objections, then at the present time this concept is generally accepted and possesses great practical value for disclosing the elastic properties of proteins and for understanding the process for the coagulation of their solutions.

According to Kurbatov, dehydration simplifies the composition and accelerates the crystallization of a polyamphion. For this reason, crystallization expands inside of polyamphions, i.e., the polyamphions are trans-formed with greater or less rapidity into crystalline polyamphions. In exactly the same manner, in order to obtain gels, it is only necessary to have a sufficiently high valence for the ions, needed to produce slow crystallization, and a sufficiently close approach to the balanced charge state. Only a slight deviation from the balanced charge state results in the formation of colloidal crystalline polyamphions. If the ions have a fairly low valence, and if the solution deviates considerably from the balanced charge state, then an ionic solution is obtained.

According to the theory of Kurbatov, gels have a structure that resembles a space lattice, the unit cells of which are filled either with water or with solution; the thickest places in the spongy tissue are the crystallization centers, while the thinnest places are either formed as the result of dehydration or ruptured as the result of hydrolysis. The substances crystallizing from a solution, a colloidal solution, or a gel, always have a simpler composition than the original solution or gel. Colloids and gels are transient formations, decomposing into crystals and solvent. According to the theory of Kurbatov "the crystal and the pure liquid are the limiting states of a substance; solutions, colloidal solutions and gels are its intermediate states" [86, 87, 95, 96, 128].

On a general plane, the crystal-polyamphion theory of Kurbatov explained the process for the formation of crystals, gels, colloids and solutions. His theory placed in one continuous series such contrasting states of substances as crystals—gels—colloids—true solutions, and established their unity. The theory also showed that crystals, gels, colloids and solutions are linked witn each other through mutual transitions. If in 1924, when V. Ya. expressed and developed the crystal-polyamphion theory, the scientific literature was almost devoid of data on the presence of crystallization centers in animal gels, then in the thirties the broad x-ray studies of colloids and tissues gave direct proof of the tenets and conclusions of the crystal-polyamphion theory. The theories of gel formation developed at a considerably later date by a number of prominent foreign investigators (Kruyt, Carman,

etc.) proved in many respects to be identical with the theory of Kurbatov. The opinions of V. Ya. regarding the processes of gel formation received further expansion in the investigations of A. V. Kiselev, who studied the active surface structure of silica gel (1936), and those of V. B. Aleskovskii (1949-1957) [7], who studied the chemical structure of substances showing both absorption capacity and catalytic activity.

Extending the crystal-polyamphion theory to biochemical phenomena, V. Ya. came to the conclusion that crystallization plays an essential role in living processes. In his opinion, the complete development of crystallization, i.e., decomposition of a gel into crystal and liquid, is one of the reasons for the death of the organism.

Mineral ions (Ca'', PO_4''') are found in the living tissue in extremely small amounts, but their importance for the processes of living is very great. As the result of a periodicity in the deposition of the calcium and sodium salts of polyamino acids in the organism there appears a periodicity in the structure of the organism's tissues [110, 121, 123]. The deposition of calcium ions in the organism's tissues leads to a contraction of the tissues (to a constriction of the blood vessels), while the deposition of sodium ions leads to increased hydrolysis of the tissues and to their swelling. All of this determines the periodicity of the phenomena of living. The periodicity of tissue structure was shown later when smooth muscle fibers were studied, in particular, using the electron microscope method.

Generalizing the theory of liquids and the crystal-polyamphion theory of colloids and gels led V. Ya. to develop the polyionic-halistic theory of electrolytes, according to which a solution is regarded as a system in which water not only acts on the electrolyte (hydrolysis), but is itself "halized" due to the influence exerted by the strong charges of the ions of the electrolyte, causing an increased asymmetry of the mutual distribution of the hydrogen and hydroxyl ions. Here the water shows increased ionization due to the constant exchange of free ions or of the ions formed as a result of the hydrolysis of the polyamphions. Upsetting the symmetry of the hydrogen and hydroxyl ions causes the water to show different degrees of ionization in different parts of the solution. Water, suffering change when an electrolyte is dissolved in it, in this manner causes the latter to change, increasing its ionic character. According to the concepts of V. Ya., ions dissolve in water as coordination complexes with the water, containing more of the latter than is present in crystallohydrates. The ions, when the concentration of the electrolyte solution is increased, or when the balanced charge state is approached, are converted into polyions. In the case where crystallization centers develop in the polyions, the latter are transformed into crystalline polyions. Monovalent ions, in harmony with their fast crystallization rate, give crystallization centers that are formed and decomposed in exactly the same manner as the polyions of the solution are formed and decomposed continuously. In electrolytes with multivalent ions the amphions, polyamphions and polyions are formed and decomposed all the time. This represents the principal difference between concentrated solutions of electrolytes and colloids.

In many respects, the basic tenets of the Kurbatov polyionic-halistic theory have found at the present time, in a different form, a confirmation and experimental expansion in investigations of polyelectrolytes.

In conclusion it should be stated that V. Ya. Kurbatov was a prominent investigator in the field of architecture and art, and was a great expert on the architecture of Leningrad and its environs. To his pen belong the widely recognized authoritative monographs: "Gardens and Parks" (1916), "St. Petersburg" (1913), "Pavlovsk" (1911), "Guide to the Suburbs of Leningrad" (1924), and "Reshetki of Leningrad" (1938). He was also the author of many brochures and articles on art and architecture [8].

Simultaneously with a large teaching and research activity, V. Ya. found time to have museums built in the former royal courts and parks found in the suburbs of Leningrad [Pushkin (formerly Tsarskoe Selo), Petrodvorts (formerly Petergof), Pavlovsk, Lomonosov (formerly Oranienbaum)]. He was one of the founders of the Leningrad Museum of History [9]. From 1918 to 1923 Kurbatov headed the management of the royal court museums and parks in Leningrad.

The life of Vladimir Yakovlevich Kurbatov is a shining example of service to his country.

LITERATURE CITED

[1] State Historical Archives of the Leningrad District, Stock 14, List 1, No. 9521, p. 1 (1900).

[2] Large Soviet Encyclopedia, 2nd ed.,Vol. 24, p. 81 (1954).

[3] State Historical Archives of the Leningrad District, Stock 492, List 2, No. 16, 820, pp. 22, 42, and 56 (1907).

[4] P. N. Ariyan, First Women's Calendar 9, 425 (1907); Supplement of Second Petrograd Polytechnic Institute, Petrograd (1923); V. Ya. Kurbatov, Nature [USSR], No. 3, 76 (1947).

[5] V. I. Semishin, Periodic Law of D. I. Mendeleev in the Studies of Russian Scientists (MIKhM Press, 1959), p. 94.*

[6] A. A. Grinberg, Supplement "Twenty-Five Years of Soviet Chemistry" (Izd. AN SSSR, 1944) p. 20.*

[7] V. B. Aleskovskii, Supplement "Concerning Chemical Kinetics, Catalysis, and Reactivity" (Izd. AN SSSR, 1955), p. 572.*

[8] A. P. Ostroumova-Lebedeva, Autobiographical Sketches ("Art" Press, 1945), Vol. 2, pp. 38, 50, 52, 67, 71, 82, 133;*(Academy of Artists of the USSR Press, 1951), Vol. 3, pp. 7, 16, 18, 22, 26, 108, 168, 181.*

[9] Architecture and Buildings in Leningrad, No. 1 (14), 48 (1957).

BIBLIOGRAPHY OF PRINCIPAL SCIENTIFIC PAPERS OF V. Ya. KURBATOV

1. Relation between the latent heat of vaporization and the vapor density. J. Russ. Chem. Soc. 34, 250, (1902).

2. Results of studying the heats of vaporization of aniline at reduced pressures. Ibid., p. 639.

3. The Trouton rule and other constants, observed at the boiling point. Ibid., p. 641.

4. The Schiff rule for change in the heat capacity of organic liquids with temperature. Ibid., p. 640.

5. The latent heat of vaporization and the heat capacity of mercury. Ibid., p. 659.

6. Study of the heat capacity and latent heats of vaporization of aniline. Ibid., p. 766.

7. The heat of vaporization of mercury, Z. physik. Chem. 43, 104 (1903).**

8. The heat of vaporization of mercury and the Trouton rule. Compt. rend. de la congres des naturalistes du Nord, Helsinfors (1903).**

9. Change in the heat capacity of organic liquids with temperature. J. Russ. Chem. Soc. 35, 119 (1903).

10. The latent heats of vaporization of organic liquids. Ibid., Physical Section, p. 158.

11. Formula for converting boiling points to normal pressure. Ibid., p. 309.

12. The Trouton rule and other constants, observed at the boiling point. Ibid., p. 319.

13. The structure of hardened steel. J. Russ. Chem. Soc. 36, 1524 (1904).

14. Contribution to the metallographic study of hardened steel. Study of etching reagents.*** Rev. met. 11, 178 (1905).

15. Contribution to the metallographic study of hardened steel.*** Rev. met. 11, 178 (1905).

16. Concerning the structure of steel. J. Russ. Chem. Soc. 37, 169 (1905).

17. The critical temperature. J. Russ. Chem. Soc. 38, Physical Section, p. 81 (1906).

18. Contemporary status of photochemistry. Ibid., p. 161.

19. Method for the preparation of austenite. J. Russ. Chem. Soc. 39, 664 (1907).

20. Proper temperatures for the crystalline state. Ibid., p. 1139.

21. Change in the Trouton constants with temperature. Ibid., p. 1140.

22. Theory of radiation. Ibid., p. 1141.

23. Rule of Dulong and Petit. Ibid., p. 1141.

---

* In Russian.
** In German.
*** In French.

24. Characteristics of the metal state and the electroconductivity of iodine. Ibid., p. 1141.

25. Heat capacity and latent heat of vaporization of acetic anhydride. Ibid., p. 1141.

26. Heat capacity of sulfur. Ibid., p. 1143.

27. Study of the vaporization of amyl ether. Ibid., p. 1143.

28. Latent heat of vaporization of p-toluidine. Ibid., p. 1144.

29. Significance of the atomistic hypothesis. Ibid., p. 1181.

30. Addition to the paper "Significance of the atomistic hypothesis". Ibid., p. 1216.

31. Change in the heat capacity of mercury. Ibid., p. 1442.

32. Importance of the theory of radiation for the theory of structure. Ibid., 1443.

33. The conception of "element". Ibid., p. 1444.

34. Structure of the sorbite-troostite components of steel. Ibid., p. 1456.

35. Concerning the solid state. Ibid., p. 1406.

36. The relationship between electric and heat conductivity. Ibid., p 1407.

37. Theories of metal conductance. Ibid., p. 1607.

38. D. I. Mendeleev. Technical Bulletin 4, 103 (1907).

39. Life and works of Mendeleev. Physical Review [USSR] 8, 1 (1907).

40. Concerning the heat capacity of mercury. J. Russ. Chem. Soc. 40, 811 (1908).

41. Concerning Avogadro — Guldberg's rule. Ibid., p. 813.

42. Concerning the ether. Ibid., 1468.

43. Latent heat of vaporization of isoamyl ether, naphthalene, isobutyl ether, acetic anhydride, and p-toluidine, and determination of the association of liquids. Ibid., 1471.

44. Change in the Trouton constants in a given homologous series. Ibid., p 1493.

45. The structure of hardened steel. Memoirs Russ. Tech. Soc. 4, 187, (1908) (jointly with M. Matveev).

46. Molecules formed by the union of identical groups. Phenomenon of association. St. Petersburg, (1908).

47. The solid state.* J. chim. phys. 6, 337 (1908).

48. Concerning the structure of hardened steel.* Metallurgie 5, 721, (1908).

49. On a polymorphous form of iodine.* Z. anorg. Chem. 56, 230, (1908).

50. Concerning the structure of hardened steel. J. Russ. Chem. Soc. 41, 1 (1909).

51. The conception of "element". Ibid., 304.

52. The heat capacity of sulfur. Ibid., p. 311.

53. Relation between molecular weight and the capillary constants. Ibid., p. 1722.

54. Concerning the association of liquids. Ibid., p. 1818.

55. Concerning the association of liquids. Ibid., p. 1422 (jointly with G. Eliseev).

56. The association of glycerin. Ibid., p. 1426 (jointly with G. Eliseev).

57. The theory of metallic conduction.** Ion 1, 306 (1909).

58. General review on the scientific activity of D. I. Mendeleev. Trans. First Mendeleev Congress, St. Petersburg, p. 36 (1909).

* In French.
** In German.
*** In English.

59. Latent heat of vaporization, heat capacity and degree of association of methyl mercaptan, ethylamine, acetyl chloride and ethylene oxide. J. Russ. Chem. Soc. 42, 1296 (1910).

60. Heat capacity, latent heat of vaporization and degree of association of diethyl malonate and acetoacetic ester. J. Russ. Chem. Soc. 43, 324 (1911).

61. On the association of liquids. J. Russ. Chem. Soc. 44, 467 (1912).

62. On calculating the surface tension of liquids. Ibid., p. 1003.

63. Latent heat of vaporization, heat capacity and association of thiophene. Ibid., p 1004.

64. On the association of liquids. Ibid., p. 1004.

65. Heat capacity and latent heats of vaporization of benzene, acetone, alcohol, and azeotropic mixture of water and alcohol. Ibid., p. 1005 (jointly with V. Goncharov and D. Volkov).

66. Heat capacity and latent heat of mercury. Ibid., 45, 659 (1913).

67. Latent heat of vaporization and heat capacity of bromoform, anthracene, ethyl chloride, ethyl bromide and ethylene bromide. Ibid., p. 660.

68. Heat capacity and latent heat of vaporization of diphenyl, quinone, chrysene, bromonaphthalene and phenol. Ibid., p. 660.

69. The Trouton— Nernst rule. Ibid., p. 661.

70. Production of Wrought Iron. Monograph. Bulletin of Bureau on Agricultural Machinery (Petrograd, 1915), p. 1.

71. The Cementation of Steel. Monograph. Bulletin of Bureau on Agricultural Machinery (Petrograd, 1915), p. 1.

72. Concerning cementation. Ibid., p. 1 (1916).

73. Study of scythes and scythe steels. Ibid., p. 1 (1916).

74. Study of the materials in plows of the Sakk type. Ibid., p. 1 (1916).

75. Report and description of laboratory studies on the testing of materials. Ibid., p. 1 (1916).

76. Possible Techniques for Carbureting Alcohol (Press of the Commission on Military and Technical Aid to United Scientific and Industrial Organizations, Petrograd, 1916), p. 1.

77. Relation between the composition, heat capacity and inner pressure of normal and abnormal liquids. J. Russ. Chem. Soc. 48, 192 (1916).

78. The Heat Capacity of Liquids. Monograph. Bull. Petrograd Technol. Inst. 24, (1916).

79. Additional data on the relationship between the heat capacity of normal liquids and the temperature. J. Russ. Chem. Soc. 50, 163 (1916).

80. Data for the heat capacity of abnormal liquids. Ibid.

81. Autowelding and Different Methods for the Welding of Metals. Monograph (Scientific Chem.-Tech. Press, Petrograd, 1919).

82. Introduction to Chemistry (Scientific Chem.-Tech. Press, Petrograd, 1919).

83. Physical Chemistry (Petrograd Technological Institute Lithograph Press 1922).

84. Principles of Chemistry (Scientific Chem.-Tech. Press, Petrograd, 1923).

85. Physical Chemistry (Military-Economy Academy of the Workers' and Peasants' Red Army Lithograph Press, Petrograd, 1924).

86. Chemistry of Colloids and Gels (Military-Economy Academy of the Workers' and Peasants' Red Army Lithograph Press, Petrograd, 1924).

87. Chemistry of Colloids and Gels (Scientific Chem.-Tech. Press, 1925).

88. D. I. Mendeleev. Survey of scientific activity. Chem. Industry [USSR] 1, No. 7, 11 (1925).

89. The Law of D. I. Mendeleev. Monograph (Sci. Chem.-Tech. Press, 1925).

90. Introduction to a Study and Practical Exercises in Physical Chemistry ("Kubuch" [Commission for Improving the Living Conditions of Students] Press, 1926).

91. Science and the Chemical Industry. Papers Delivered at the First All-Union Convention on Problems Relating to the Chemical Industry, p. 1 (1926).

92. Scientific Creativity of D. I. Mendeleev (Bureau of Weights and Measures Press, 1926).

93. Chemical Analysis. Technical Encyclopedia, Vol. 1, p. 585 (1927).

94. Chapter "Chemistry" in the book Ten Years of Soviet Science (Gosizdat, 1927), p. 189.

95. Properties and Structure of Liquids. Monograph. Bull. Lensovet Leningrad Technological Institute (1927).

96. Physicochemical Theories and Their Application in Industry. Part 1 (1927) and Part 2 (1929).

97. The Nature of the Association of Liquids. Activation and Structure of Molecules *(Paris, 1928), p. 473.

98. Advances in Colloid Chemistry ("Worker in Education" Press, Leningrad, 1928).

99. Material for the study of the drying process of glue. J. Chem. Ind. (Moscow) 7, 458 (1930) (jointly with M. Kurylev).

100. Problems of the Technology of Alloys in the Next Ten Years (Scientific Chem.-Tech. Press, 1929).

101. Contemporary trends of world chemical thought. Bulletin of the Scientific Commission of the Committee on Chemisation of the Council of Soviet Commissars of the USSR (1929).

102. Chemistry through four centuries. Supplement of Committee on Chemisation (Scientific Chem.-Tech. Press, 1929), pp. 25--70.

103. Foreword and annotations to the book by M. Urben, The Chemical Element and the Atom (Scientific Chem.-Tech. Press, 1929), pp. 1--9.

104. Science -- the Foundation of the Chemical Industry (Scientific Chem.-Tech. Press, 1929).

105. Concerning scientific research studies for the chemical industry. Chemistry and Economy [USSR] 3, 5 (1930).

106. The plant laboratory and the development of new ideas and processes in chemical technology. Ibid., p. 91.

107. Development of Colloidal Chemistry and Method of Improving the Lacquer Paint Industry (Scientific Chem.-Tech. Press, Leningrad, 1930).

108. Recent Studies in the Domain of Colloidal and Physical Chemistry and Their Application to the Problems of Paper Sizing. Themes of Reports (Scientific Council of the Lensovet Chem.-Tech. Inst. Press, Leningrad, 1930), p. 152.

109. Revision and additions to the book by D. A. Vil'son Chemistry of Leather (Scientific Chem.-Tech. Press, Leningrad, 1930), pp. 1 - 54.

110. Materials relating to the problem of seed stimulation. Trans. Inst. Applied Botany, Genetics and Selection, V. I. Lenin All-Union Academy of Agricultural Sciences 23, 155 (1930).

111. The influence of inorganic ions on the properties of seed.* *Protoplasma 11, 34 (1930) (jointly with S. Gluckmann).

112. Relation between the heat capacity of liquids and the temperature. Themes of papers delivered at 5th Mendeleev Congress, Leningrad, 1930.

---

* In French.

** In English.

113. Methodical Course in Physical Chemistry (Lensovet Leningrad Chem.-Tech. Inst. Press, 1930).

114. Methodical Course on the Chemistry of Colloids and Gels. Ibid., 1930 .

115. Colloidal chemistry in the paper industry. Paper Industry [USSR] Nos. 2 - 3, 6 (1930).

116. Chemical Stability of Materials and Their Protection From Corrosion. Monograph (Scientific Chem. -Tech. Press, Leningrad, 1930).

117. Revision and additions to the book by G. Glasser, Introduction to the Science of Tanning, and Colloid Chemistry in the Tanning Industry (Scientific Chem.-Tech. Inst. Press, Leningrad, 1931).

118. Concerning the theory of gelatinization.* Koll.-Z. 55, 70 (1931).

119. D. I. Mendeleev. Nature [USSR] 2, 101 (1931).

120. D. I. Mendeleev and the science of silicates and glass. Ceramics and Glass (USSR), Nos. 5 - 6, 2 (1931).

121. Crystal-polyamphionic theory of life and the origin of life. Communications on Scientific-Technical Studies in the Republic [in Russian] 31, 119 (1932).

122. Crystal-polyamphionic theory of colloidal, gelatinous and ionic solutions. Ibid., p. 120.

123. Speech given at the opening of the Likvorologicheskoi Laboratory. Archives Biological Sciences [USSR] 32, 871 (1933).

124. The ideal equilibrium and the possibility of approaching it experimentally. Trans. Conference on Phys.-Chem. Analysis, p. 28 (1933).

125. Editor-in chief of the 2nd Edition of the volume "Papers of D. I. Mendeleev" (Goskhimtekhizdat, Leningrad, 1934).

126. Basic conditions for the sure metallic protection of metals. Trans. First Conference on Corrosion of Metals (Izd. An SSSR, 1934), p. 26.

127. Basic conditions for reliable nonmetallic coatings. Ibid., p. 30.

128. The law of D. I. Mendeleev and principles of classification in chemistry. Jubilee Mendeleev Congress (Goskhimtekhizdat, 1934).

129. Complete theory of electrolytes and storage battery processes. Supplement of Scientific Research Studies on Chemical Sources of Current (Central Laboratory for Storage Batteries Press, 1934). p. 5.

130. Influence of time and solution composition on the potential of nickel. Trans. Lensovet Leningrad Chem.-Tech. Inst. 5, 119 (1935) (jointly with P. Myshkovskii).

131. Vapor pressure of nitrocellulose solutions. Plastic Materials [USSR] 1, 1 (1935).

132. Processes for the solution of cellulose derivatives. Supplement "Plastic Materials" (Khimteoretizdat, 1935). pp. 3—76.

133. Effect of cations on electrode potentials of alkali amalgams. Trans. Lensovet Leningrad Chem.-Tech. Inst. 2, 60 (1935) (jointly with V. Alekseev).

134. Basic processes at the interface metal—solution and electrode potentials. Supplement of Scientific Research Studies on Chemical Sources of Current (Central Laboratory for Storage Batteries Press, 1935), 2, p. 3.

135. On the solubility of colloid—gelatinous precipitates. Trans. Lensovet Leningrad Chem.-Tech. Inst. 3, 1 (1936).

136. Editor-in-chief of the 3rd Edition of the volume "Papers of D. I. Mendeleev" (Khimteoretizdat, Leningrad, 1936).

137. Editor-in-chief of the 4th Edition of the volume "Papers of D. I. Mendeleev" (Khimteoretizdat, Leningrad, 1937).

---

* In German.

138. The potentials of nickel in sulfate solutions. Trans. Lensovet Leningrad Chem.-Tech. Inst. $\underline{4}$, 108 (1938) (jointly with P. Myshkovskii).

139. Complete theory of electrolytes and storage battery processes. Supplement of Scientific Research Studies on Chemical Sources of Current (Central Laboratory for Storage Batteries Press, 1938), $\underline{4}$, p. 5.

140. Influence of electrolytes on the gelation of cosolutions with aluminum hydroxide. Trans. Lensovet Leningrad Chem.-Tech. Inst. $\underline{9}$, 119 (1940).

141. Diffusion of dyes and the size of their crystalline polyions. Ibid., p. 15 (jointly with T. Renzina).

142. The dependence of the adsorption of dyes by wool and cotton on pH. Ibid., p. 15 (jointly with A. Moiseev).

143. Half-gels. Ibid., p. 113 (jointly with S. Vol'fson).

144. Dependence of the crystal form of alums on the solution pH. Ibid., p. 125 (jointly with A. Moiseev).

145. Study of the cosolution of fish glue. Ibid., p. 134 (jointly with E. Mandel'shtamm and I. Rabinovich).

146. Polyionic-halistic theory of electrolytes. Themes of Papers Delivered at the Scientific-Technical Conference of Lensovet Leningrad Chem.-Tech. Inst., p. 11 (1946).

147. The state of water in electrolyte solutions. Ibid., p. 11.

148. Dependence of heat properties of liquids on the temperature. Trans. Lensovet Leningrad Tech. Inst. $\underline{13}$, 1 (1947).

149. Women's polytechnical courses and the first women engineers. Nature [USSR] $\underline{3}$, 76 (1947).

150. Heat capacities of liquids. I. Heat capacities of benzene hydrocarbons. J. Gen. Chem. $\underline{18}$, 1999 (1948)*.

151. Heat capacities and dependence of the heat capacities of halogen derivatives of acyclic hydrocarbons on the temperature. J. Gen. Chem. $\underline{18}$, 972 (1948). [USSR].

152. Editor-in-chief of the 15th Edition of the volume "Papers of D. I. Mendeleev" (Izd. AN SSSR, 1949).

153. Heat capacities of liquids. The heat capacities of hydrocarbons with several noncondensed rings. J. Gen. Chem. 20, 1139 (1950).*

154. The nature of crystals. The interatomic linkage of halogen compounds. J. Gen. Chem. $\underline{20}$, 958 (1950).*

155. The nature of crystals. Interatomic linkage and the solubility of salts. Ibid., p. 1333.*

156. The nature of crystals. The interatomic linkage of oxides and their hydrates. Ibid., p. 1543.*

157. The nature of crystals. The interatomic linkage of sulfur compounds. Ibid., 1549.*

158. The nature of crystals. The interatomic linkage of organic crystals and the mutual solubility of organic substances. Ibid., p. 1760.

159. Comparison of thermal data for characterizing the liquid state. Themes of Papers Delivered at the Scientific-Technical Conference of the Lensovet Leningrad Technical Institute, p. 17 (1950).

160. Intermolecular cohesion of liquids. Ibid., p. 20 (1951).

161. Rules observed for latent heats of fusion. Ibid., p. 32.

162. Heat capacity of crystals. Ibid., p. 31.

163. Perfecting the formulas of D. P. Konovalov. Paper Delivered at the Scientific-Technical Conference of the Lensovet Leningrad Technical Institute, p. 14 (1952) (jointly with N. Lebedeva).

164. Unusual cases of the cocrystallization of corundum and α-copper alloys. Ibid., p. 17.

165. Editor's note and revision of the papers "Specific Volume" and "The Periodic Law" in the 25th Edition of the volume "Papers of D. I. Mendeleev" (Izd. AN SSSR, 1952).

---

* Original Russian pagination. See C. B. Translation.

STUDY OF PECULIAR CASES OF STRATIFICATION OF LIQUIDS

I. L. Krupatkin

Ivanov Chemical-Technological Institute

One of the more important rules holding in any liquid of a ternary system showing stratification, is the tenet that, on the stratification isotherm, the conodes and median line represent a single geometric complex at the critical point of isothermal solution. This complex is associated with chemical interaction in the ternary system and is located in its composition triangle as follows. a) The critical point of the binodal curve is shifted away from the dominant binary system. b) The conodes fan out toward the dominant system (at times this holds for only a portion of the conode [1]). c) The median line is deflected by a certain angle away from the dominant system [2].

Nevertheless, investigation of the ternary system $AgNO_3$—NaBr—KCl by N. S. Dombrovskaya and E. A. Alekseeva [3] revealed that in it the entire geometric complex described above is turned by 90° from its normal position. Analysis of this astonishing fact, remaining unexplained in the literature, leads to the conviction that similar peculiar cases of stratification of liquids in systems are associated with the formation of compounds that decompose into two liquid phases when melted. A total of only several binary systems in which the indicated type of compounds arises is described in the literature. Belonging in this category are, for example: the organic system triphenylmethane—m-phenylenediamine [4,5]; the metallic systems Mg—Ni [6], K—Zn, Na—Zn, K—Pb, Al—Ca, Cd—Ca, Na—Fe, Hg—I_2 [7]; the salt systems KCl—$AgNO_3$ [8], NaBr—$AgNO_3$ [9]; and the systems containing the hydrates of the gases: SO_2—H_2O, and HBr—H_2O [10]. The mentioned ternary system, containing the same type of compounds, is apparently the only one reported in the literature.

The purpose of the present study was to determine the reasons for the formation and nature of the described compounds, and also the manner of their behavior in solutions (i.e., in ternary systems), leading to peculiar cases of stratification of liquids.

EXPERIMENTAL

To study the discussed problem we selected the ternary system chloral hydrate—diethylamine—water. The binary systems composing it are characterized by the following data.

The system chloral hydrate—water was studied by both the fusion [11] and the viscosity [12] methods. The fusion curves show the presence of a compound (melting at -1.4°) that is composed of 1 molecule of chloral hydrate and 7 molecules of water. The viscosity curves for the system chloral—water show, even at 50°, only chloral hydrate. As a result, the heptahydrate is dissociated in the liquid phase of the system chloral hydrate—water. This is the reason for the observation that stratification occurs when a chloral—water system, containing 40—60% mole % chloral is heated to 175—190° [13].

The system diethylamine—water was studied by the stratification method [14]. The stratification curve has a lower critical point (143.5°), determined by the dissociation of the unstable hydrates of diethylamine.

The system chloral hydrate—diethylamine was investigated in the present study as being a system in which a compound melting with stratification is formed. It was assumed that the interaction of the components in this system would be similar to the behavior exhibited by the system triphenylmethane—m-phenylenediamine, in which each component has dual and opposite functions with respect to the other component; on the one hand,

TABLE 1

Equilibrium of Liquid Phases in the System Chloral Hydrate, Diethylamine

Chloral hydrate (wt. %)	Stratification temperature
58.50	No stratification at 15°
58.60	20.0
59.00	58.0
60.00	66.0
61.00	89.0
63.00	105.0
65.00	112.0
67.00	113.0
69.00	110.0
71.00	92.0
73.00	74.5
75.00	48.0
76.00	25.0
76.50	No stratification at 15°

TABLE 2

Compositions of the Ternary Mixtures, Corresponding to the Points on the Isotherm (at 20°) of the System Chloral Hydrate —Diethylamine —Water (in Wt. %)

Left portion of the isotherm			Right portion of the isotherm		
chloral hydrate	diethylamine	water	chloral hydrate	diethylamine	water
58.60	41.40	—	76.00	24.00	—
56.97	41.87	1.16	75.46	23.00	1.54
54.90	42.21	2.89	74.34	21.75	3.91
51.69	42.57	5.74	73.26	18.60	8.14
46.24	42.20	11.56	68.80	14.00	17.20
40.77	41.76	17.47	60.90	13.00	26.10
35.40	41.00	23.60	53.24	11.27	35.49
30.00	40.00	30.90	45.08	9.83	45.09
24.00	40.00	36.00	36.60	8.51	54.89
18.54	38.19	43.27	27.64	7.86	64.50
12.88	35.61	51.51	18.80	6.00	75.20
6.91	30.90	62.19	9.50	5.03	85.47
3.72	25.57	70.71	4.79	4.13	91.08
2.42	19.16	78.42	2.86	4.54	92.60

Fig. 1. Equilibrium of liquid phases in system chloral hydrate —diethylamine. K is the critical point. Explanation in text.

they combine with each other (triphenylmethane is very susceptible to adding different compounds [15], including certain aromatic amines [16]), and on the other hand, many mixtures of hydrocarbons with amines are inclined to stratify (this property is used in practice to determine the aniline points of benzines [17]; in particular, mixtures of triphenylmethane with ammonia show stratification [18]). In view of the above mentioned properties, triphenylmethane and m-phenylenediamine react with each other to form a compound that decomposes into two liquid phases when melted. The components of the system chloral hydrate —diethylamine have analogous properties. On the one hand, chloral hydrate has the function of a halo derivative of the hydrocarbon; this function weakens its interaction with diethylamine and leads to their stratification, which is also known for several other hydrocarbons and amines: for example, methyl iodide and pyridine behave in such manner [19]. On the other hand, chloral hydrate has the properties of an aldehyde and a definite acidic function; it adds ammonia [20] and certain amines [21, 22]. The above, therefore, made it possible to postulate that the reaction of chloral hydrate with diethylamine would result in the formation of a compound melting with stratification.

For the study we took the following reagents: pharmaceutical grade chloral hydrate, m.p. 48.0°, as dry colorless crystals; diethylamine, dried and freshly distilled, taking the fraction with b.p. 55.5°. The reaction of chloral hydrate with diethylamine is strongly exothermic, and for this reason their mixing was done under cooling. The visual-polythermal method of V. I. Alekseev [23] was used to study stratification, using sealed glass ampules and a glycerin thermostat. Crystallization in the system was not studied due to the high degree of supercooling. The numerical data obtained are given in Table 1, while the stratification polytherm is shown in Fig. 1.

As Fig. 1 shows, the stratification curve consists of two branches, both rising very sharply with increase in the temperature and merging in the upper critical point K at 113.5°, corresponding to 67.00% chloral hydrate. (The chloral hydrate specimen, obtained as coarse crystals with a light brown tinge, has nearly the same melting point as the pure product, but forms a critical point at 93°, i.e., some 20° lower). On each branch of the binodal curve, increasing the temperature by 90° increases the mutual solubility of the liquid phases by a total of 6%,

Fig. 2. Solubility isotherm at 20° for the tenary system chloral hydrate—diethylamine—water. K is the critical point of isothermal solution, and AK is the median line. Explanation in text.

Fig. 3. Graph for determining the conodes (homogenization curve). Explanation in text.

The lower portions of the branches are found in the region of metastable stratification. The binodal curve defines a very narrow and tall region of stratification, almost in the middle of which is located the ordinate, belonging to the composition where the molecular ratio of the components is 1:1 (69.34% chloral hydrate). The critical point K is shifted from the ordinate toward the lower melting component (diethylamine) by 2.34% (a similar shift and in the same direction also occurs in the system triphenylmethane—m-phenylenediamine). As a result, the indicated thermochemical data and the described properties of the stratification region show that a compound having a 1:1 molecular ratio of the components, and melting with the formation of two liquid phases, is formed in the system chloral hydrate—diethylamine. The behavior of this system in the ternary system with water (see below) confirms this fact. The obtained compound contains 7.56% of chemically bound water.

As will be seen below, hydration of this compound stabilizes it in the liquid phase. This circumstance, determined in preliminary experiments, was the reason for selecting water as the third component in studying a ternary system.

The ternary system chloral hydrate—diethylamine—water was examined for stratification by isothermal titration at 20° (double-distilled water was taken). For this purpose we studied 13 sections, proceeding from the diethylamine corner along the side of the binary system chloral hydrate—water, containing respectively 2, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 95 and 97% of water. The section containing 97.5% water failed to show stratification. The compositions of the mixtures corresponding to the points on the isotherm are given in Table 2; the stratification isotherm is plotted in Fig. 2.

As Fig. 2 shows, the stratification isotherm bounds a narrow region of liquid-phase equilibria, situated along the quasi-binary section of the compound with a 1:1 composition. Only when the mixtures contain more than 85% water does the stratification region deviate slightly from the quasi-binary section toward the side of the system water—diethylamine. As has been mentioned, the binodal system chloral hydrate—diethylamine is shifted toward the side of the latter. These two phenomena are related, in that the deviation of the isotherm is explained by the influence exerted by the binary system on the character of the ternary system. The stratification region begins from the break in the solubility of the binary system chloral hydrate—diethylamine, extends through the entire composition triangle, and ends near the water corner. As a result, water exerts a very weak homogenizing effect on stratification in the system chloral hydrate—diethylamine. Consequently, water takes very little part in the dissociation of the compound of the given binary system. To the contrary, hydration of this compound stabilizes it in the liquid phase. Near the side of the system chloral hydrate—diethylamine the mutual solubility of the liquid phases increases, as a result of which the portions of the isotherm lying on both sides of the quasi-binary section come somewhat closer to each other.

The conodes for the stratification isotherm, studied at 20°, were determined by the isothermal method, employing the technique of homogenizing the mixtures corresponding to the points on the isotherm by dilution with

TABLE 3

Compositions of Mixtures for
Determination of Conodes
(Homogenization Curve)

Diethyl consumed for homogenization (in wt. %)	Amount of diethylamine in the layer (in wt. %)	
	upper layer	lower layer
6.42	25.57	—
9.97	31.40	—
12.55	35.61	—
16.00	—	39.50
16.84	—	40.00
18.51	—	40.83
19.73	—	41.67
21.18	—	41.68
22.30	—	40.00
25.91	—	33.00
29.40	—	26.00
31.47	—	21.70
32.68	—	18.66
33.80	—	14.00
34.19	—	12.74

TABLE 4

Compositions of Coexisting Phases at 20° in the Ternary
System Chloral Hydrate—Diethylamine—Water (in Wt. %)

Upper layer			Lower layer		
chloral hydrate	diethyl-amine	water	chloral hydrate	diethyl amine	water
9.00	33.50	57.50	41...	41.50	17.00
7.00	30.00	63.00	55.00	42.00	3.00
5.50	29.00	65.50	63.30	36.70	—
4.50	27.00	68.50	66.50	33.50	—
3.50	24.50	72.00	71.00	29.00	—
2.50	22.00	75.50	73.00	27.00	—
2.30	21.00	76.70	75.50	24.50	—
2.00	17.50	80.50	75.00	22.00	3.00
2.00	11.50	86.50	74.70	21.00	4.30
2.00	7.00	91.00	73.50	19.00	7.50
3.50	4.50	92.00	71.00	16.00	13.00

one of the components [24]. In preparation for this we first determined the relationship between the amount of diethylamine in homogeneous mixtures corresponding to the binodal points, and the amount of diethylamine consumed for homogenization of the starting mixtures, diluted in half (i.e., made heterogeneous) with water. The obtained numerical data are given in Table 3, while the indicated relationship is plotted in Fig. 3. For some of the mixtures, the figurative points of which are located on the isotherm to the right of the quasi-binary section and close to the water corner, such a relationship could not be determined, since they became homogeneous when diluted in half with water. If the ability of doubly diluted compositions on the isotherm to homogenize is considered a property, then the curve in Fig. 3 is a property curve, since it expresses the relationship between a property of mixtures and the amount of one of the components in them.

On the basis of the obtained relationship we found 11 conodes, distributed uniformly throughout the entire stratification region. For this we prepared a number of heterogeneous mixtures, containing 40% water and respectively 23, 25, 28, 30, 33, 35, 37, 40, 43, 46, and 48% chloral hydrate; from these mixtures we removed samples of the investigated layer, diluted the sample with an equal amount of water, and then homogenized with diethylamine. From the amount of diethylamine consumed for homogenization, using the curve for the given layer in Fig. 3, we determined the composition of one of the layers. The composition of the second layer was found graphically by the point of intersection of the binodal with the extension of the straight line, connecting the obtained composition with that of the original heterogeneous mixture. The compositions of the coexisting phases are given in Table 4, while the conodes are plotted on the isotherm in Fig. 2. As Fig. 2 shows, most of the conodes fan out toward the side of the binary system chloral hydrate—diethylamine. Nevertheless, a portion of the conodes, corresponding to the original heterogeneous mixtures, and found to the right of the quasi-binary section, show an opposite arrangement.

Figure 2 shows that the conodes in our system are located perpendicular to their normal position, exactly the same as in the system AgNO₃—NaBr—KCl. The fact that a similar result was obtained by different authors, at different times, on different specimens, is additional indirect proof that systems with the described arrangement of the conodes exist. Only the difficulty of explaining these systems remains, which will be discussed below. The presence of solutropism in the system chloral hydrate—diethylamine—water is also evidence that the arrangement of the conodes shown in Fig. 2 is valid.

To determine the composition of the critical point of isothermal solution from the property curve we used the method of V. F. Alekseev [1, 25], modified by using the ability of mixtures to homogenize as the property. For this the compositions of the coexisting phases were plotted on the property curve (Fig. 3) and connected by
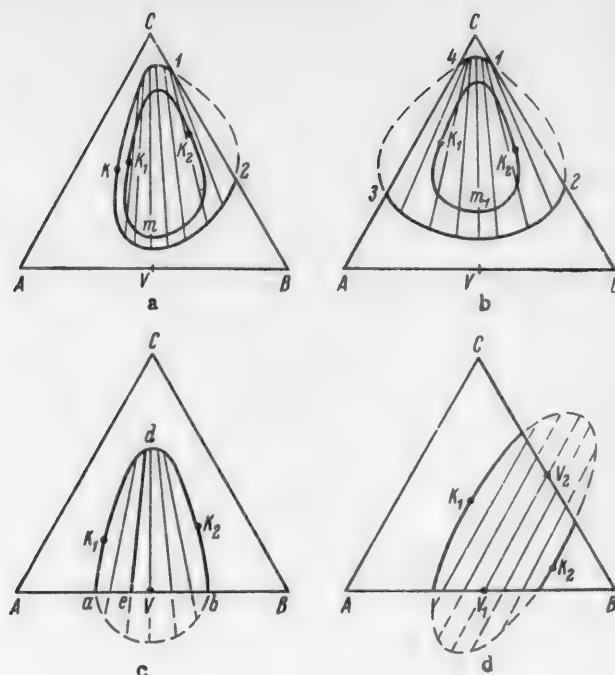
Fig. 4. Scheme for the formation of peculiar cases of stratification of liquids of ternary systems. K is critical point, V is compound, and $\underline{e}$, $\underline{d}$ is conode. Explanation in text.

straight lines. The medians of these lines lie on the straight line mK, intersecting the property curve at critical point K. This method does not require additional measurement of the homogenization property, since it is determined in the process of finding the stratification isotherm. On the other hand, it has the disadvantage that homogenization cannot be determined for all of the points on the isotherm, since some mixtures suffer homogenization even when diluted. It is specifically for this reason that the critical point K was determined only for that portion of the binodal that lies to the left of the quasi-binary section (Fig. 2). The position of the critical point on the binodal was verified by drawing the conode median line AK (Fig. 2). It is interesting that the median line repeats the shape of the imaginary portion of the isotherm (shown by the broken line), and not the linear portion of the isotherm, lying on the side of the binary system chloral hydrate—diethylamine. Both the median line and the critical point deviate away from the latter.

The above described arrangement of the conodes, the position of the critical point, and the deflection of the median line, all establish the important fact that the binary system chloral hydrate—diethylamine is dominant in the ternary system chloral hydrate—diethylamine—water. At the same time, it was experimentally shown for the first time that binary systems exhibiting both the formation of chemical compounds and stratification, in which the compositions of the compounds lie within the concentration intervals of the solubility breaks, can be the dominant systems at stratification temperatures.

This astonishing fact can be explained and demonstrated theoretically in the following manner. In a ternary system the general shape of the equilibrium isotherm for two liquid phases is a closed curve (Fig. 4a, Curve K_1K_2m). The latter, depending on the nature of the components in the system, on the manner in which they and their mixtures interact, and also on external factors (for example, temperature), can occupy a variable position in the concentration triangle of the ternary system. Up to now, ternary systems with the following positions of the stratification isotherm were studied.

1) The stratification isotherm did not reach the sides of the binary systems (Fig. 4b, Curve K_1K_2m).

2) The stratification isotherm reached the sides (of either one or both) of the binary systems, leaving the dominant system homogeneous (Figs. 4a and 4b, Curves 1K2 and 1, 2, 3, 4). •

3) The stratification isotherm reached the sides of the dominant system (or of still another system), leaving homogeneous the concentration interval in which a compound is formed in it.

This last case exists in a number of silicate-containing ternary systems [26] (for example, $FeS-FeO-SiO_2$ [27], containing binary systems in which a compound is formed in one concentration interval, and a region of stratification in another. In principle, such systems do not introduce anything new into the types of systems shown in Figs. 4a and 4b: their triangulation leads to the depicted types of ternary systems; in them, the same as in systems with three liquid phases, the geometric complex, conodes—critical point—median line, shows the normal location, the same as in the systems shown in Figs. 4a and 4b.

However, under no condition do the indicated cases limit the position of the stratification isotherm. The stratification isotherm can also be located as is shown in Figs. 4c and 4d, where A—B is the dominant system. Ternary systems of the last two types are possible in those cases where a compound which melts, forming two liquid phases, is formed in the dominant system (Fig. 4c), or where such a compound is also formed in one of the other systems (Fig. 4d). The first of these two types of systems exists in the present study, while the second type exists in the system $AgNO_3-NaBr-KCl$ [3]. In the latter ternary system, the exchange products formed in the binary systems containing $AgNO_3$ melt with stratification. The location of the conodes permits asserting that, in the liquid state, the system $AgNO_3-KCl$ is the dominant one.

Ternary systems of the discussed type create the impression that three-phase liquid equilibria should arise in them. However, in the systems $AgNO_3-NaBr-KCl$ and chloral hydrate—diethylamine—water the equilibrium of only two liquid phases was observed at the investigation temperatures. In the last system a three-phase liquid equilibrium does not arise even if the temperature is increased or lowered somewhat, although it is possible for three liquid phases in equilibrium to be formed in such systems with large changes in temperature.

A two-phase liquid equilibrium arises in the described systems as the result of isothermal processes, somewhat analogous to the described case, lying intermediate between the four-phase eutectic and the four-phase peritectic equilibria in ternary systems [28]. This analogy is based on the fact that compounds, melting with stratification, behave in a dual manner in ternary systems: as compounds melting congruently and as compounds melting incongruently. In connection with this it is possible to offer two explanations, not excluding other explanations, for the formation of a two-phase liquid equilibrium in the studied ternary systems.

1. In a ternary system A—B—C (Fig. 4c), corresponding to the one investigated in the present study, above the synthetic temperature (or in the metastable state), the reversible isothermal reaction $e \rightleftharpoons a + b$ takes place between three liquid compositions on line a,e,b. The direction of this reaction depends on the presence or the absence of component C, and consequently, also on the presence or the absence of liquid phase d, which is formed with the involvement of C. If phase d is absent, the reaction goes to the right, liquid e disappears, and the two-phase equilibrium $a \rightleftharpoons b$ arises. If phase d is present, the reaction goes to the left, and both liquids a and b disappear. Phase e is formed here, which corresponds to the equilibrium phase d, and the two-phase equilibrium $e \rightleftharpoons d$ arises on conode e,d. Phase e is formed in the first process in view of its combining in the second process.

2. For the second explanation it is necessary to assume that the line a,b (Fib 4c) represents a degenerate triangle of the three-phase liquid equilibrium. This assumption is based on the possibility of a three-phase liquid state existing in the described systems. Then, making use of the described analogy of the given systems with the intermediate case lying between four-phase eutectic and four-phase peritectic equilibria [28], we have the reversible isothermal reaction $a + b \rightleftharpoons e + d$ between four liquid solutions in the triangle a,e,b,d. Its direction depends on the addition or removal of component C, the involvement of which results in the formation of liquid phase d. If component C is added, the equilibrium shifts to the right, solutions a and b disappear, and the two-phase equilibrium $e \rightleftharpoons d$ arises. If component C is removed, the equilibrium shifts to the left, solutions e and d disappear, and the two-phase equilibrium $a \rightleftharpoons b$ is formed.

In a similar manner, it is possible to explain the creation of a two-phase liquid equilibrium in the system $AgNO_3-NaBr-KCl$, corresponding to the type depicted in Fig. 4d.

_____

•An exception are the systems with three liquid phases in equilibrium, which are not discussed in the present study.

A study of similar systems (and of compounds melting with stratification) is of great interest, and the present paper is only a start, for which reason investigations along this line are being continued.

SUMMARY

1. Stratification in the binary system chloral hydrate—diethylamine was studied. In this system a chemical compound with a 1:1 molecular ratio of the components is formed, which melts with the formation of two liquid phases. The reasons for the formation of such compounds, and the properties required by the components to cause their interaction with the formation of such compounds, were determined.

2. Stratification in the ternary system chloral hydrate—diethylamine—water was studied at 20°. This system was found to exhibit a region of a two-phase liquid equilibrium, beginning from the solubility break in the binary system chloral hydrate—diethylamine, and situated along the quasi-binary section; this region becomes homogeneous near the water apex.

3. The conodes and one of the two critical points were determined for the stratification isotherm. The conodes fan out toward the side of the system chloral hydrate—diethylamine, while the critical point and the median line are deflected away from this system.

4. From the location of the conodes, critical point, and median line it was shown that in the ternary system chloral hydrate—diethylamine—water the binary system chloral hydrate—diethylamine is the dominant one. At the same time, it was experimentally shown for the first time that binary systems in which the compositions of the compounds formed in them lie within the concentration intervals of the breaks in the solubility, can be the dominant systems at the stratification temperatures.

5. A scheme was given for the formation of ternary liquid systems containing dominant systems in which compounds melting with stratification are formed. This new type of ternary systems was studied experimentally. For such ternary systems a theoretical explanation was given for the creation of a two-phase liquid equilibrium.

LITERATURE CITED

[1] N. A. Izmailov and A. K. Franke, J. Phys. Chem. [USSR] 29, 263 (1955).

[2] I. L. Krupatkin, J. Gen. Chem. 25, 2023 (1955).*

[3] N. S. Dombrovskaya and E. A. Alekseeva, J. Inorg. Chem. [USSR] 1, 2052 (1956).

[4] Kremann, Odelga, K. Zadowsky, Monatsh. 42, 117 (1921).

[5] Kremann, Mauermann, Müller, Rösler, Monatsh. 43, 321 (1922).

[6] V. Ya. Anosov and S. A. Pogodin, Principles of Physicochemical Analysis [in Russian] (Izd. AN SSSR, 1947).

[7] G. Tammann, Manual on Heterogeneous Equilibria [Russian translation] (ONTI, Leningrad, 1935).

[8] I. A. Kablukov, J. Russ. Chem. Soc. 37, 335 (1905); 39, 914 (1907).

[9] A. G. Bergman and M. A. Zakharchenko, Trans. Novocherkassk Polytechnical Inst. (1953).

[10] G. Tammann, Metallography [Russian translation] (State United Press, Leningrad, 1937).

[11] C. van Rossem, Z. physik. Chem. 62, 711 (1908).

[12] N. S. Kurnakov and N. N. Efremov, J. Russ. Chem. Soc. 45, 329 (1913).

[13] E. Werner, J. Chem. Soc. 85, 1376 (1900).

[14] W. Aleksejeff, Ann. der Physik und Chemie [N. F.] 28, 305 (1886).

[15] W. A. Waters, Chemistry of Free Radicals [Russian translation] (IL, 1948).

[16] H. Hartley, N. Thomas, J. Chem. Soc. 89, 1013 (1906).

[17] Testing Methods for Petroleum Products [in Russian] (Gostoptekhizdat, Moscow—Leningrad, 1953).

---

*Original Russian pagination. See C. B. Translation.

[18] M. G. Tsentnershver, J. Russ. Phys. Chem. Soc. 35, 742, 897 (1903).

[19] A. H. W. Aten, Z. physik. Chem. 54, 124 (1906).

[20] A. F. Holleman, Course in Organic Chemistry [Russian translation] (ONTI, Moscow, 1937).

[21] A. Hantzsch, Ber. 25, 702 (1892).

[22] D. E. Tsakalotos, Bull. soc. chim. France 13, 281 (1913).

[23] V. F. Alekseev, J. Russ. Chem. Soc. 8, 249 (1876).

[24] R. V. Mertslin, J. Gen. Chem. 6, 1828 (1936).

[25] N. A. Izamailov and A. K. Franke, J. Phys. Chem. [USSR] 29, 120, 620 (1955).

[26] D. S. Belyankin, V. V. Lapin, and N. A. Toropov, Physicochemical Systems in Silicate Technology [in Russian] (Industrial Construction Press, Moscow, 1954).

[27] Ya. I. Ol'shanskii, Proc. Acad. Sci. USSR 59, 513 (1948); 70, 245 (1950).

[28] D. A. Petrov, Ternary Systems [in Russian] (Izd. AN SSSR, 1953).

PHYSICOCHEMICAL STUDY OF THE SYSTEM HYDRAZINE—PHENOL

I. M. Bokhovkin

Archangel Technical Institute of Forestry

Up to now the intermolecular hydrogen bond was studied as a bond between like molecules and hardly any study was devoted to compounds having the hydrogen bond between unlike molecules. At the same time, a study of compounds having the hydrogen bond between unlike molecules possesses great importance for formulating and expanding the concepts of the hydrogen bond. Compounds with hydrogen bonding between unlike molecules can be shown via the method of physicochemical analysis, which makes it possible to establish the presence of the compounds without isolating them in the free state, both at the boundary of two phases, and in the homogeneous molten state.

In this paper we present the experimental data obtained in making a physicochemical study of the system hydrazine—phenol, in which a compound exhibiting the intermolecular type of hydrogen bonding is formed. It was interesting to trace the manner in which the indicated compound plots on the composition—property diagram.

Our investigation was made using the physicochemical methods of thermal analysis, density, viscosity, surface tension, and specific electroconductance.

EXPERIMENTAL *

Hydrazine was obtained by the dehydration of the monohydrate in a nitrogen stream [1], and was purified by 3-fold distillation. The phenol was also purified by 3-fold distillation. After purification, both the hydrazine and the phenol had constants that were in good agreement with the literature data.

The visual-polythermal method was used to determine the crystallization temperatures. For each solution, the melting point of the first crystals when cooling and the disappearance of the last crystals when heating were determined, until the difference between the indicated temperatures was less than one degree.

The homogeneous phase was studied at 65, 75, and 85°. The viscosity was determined using an Ostwald viscosimeter, and was expressed in centipoises. The electroconductance was measured by the Kohlrausch method in a closed vessel fitted with smooth platinum electrodes, and was expressed in $\text{ohm}^{-1} \cdot \text{cm}^{-1}$. An audio-frequency lamp generator equipped with amplifier served as the source of current. The surface tension (dynes/cm) was investigated by the method of the highest pressure of a gas (air) bubble [2]. The vessel used in the investigations was of the closed type. Mercury was used as the sealant between the cover having the capillary tip, and the vessel. A screw arrangement was used to lower the capillary tip. The pressure was read on a toluene manometer. The hydrostatic suspension method was used to determine the density. Platinum served as the suspended material.

The data obtained in studying the fusion are given in Table 1 and plotted in Fig. 1. It was established that the system contains a compound with the composition $N_2H_4 \cdot 2C_6H_5OH$, which is characterized by having a higher melting point than either of the pure components. The first eutectic point corresponds to 12 mole % C_6H_5OH and a temperature of -18°, and the second corresponds to 90 mole % C_6H_5OH and a temperature of +28°.

The results of determining the density are given in Table 2 and plotted in Fig. 1. The density isotherms represent curves with a maximum. The maximum is found at a component ratio of 1 : 2, which corresponds to the formula $N_2H_4 \cdot 2C_6H_5OH$.

* E. O. Vitman took part in the experimental portion of this study.
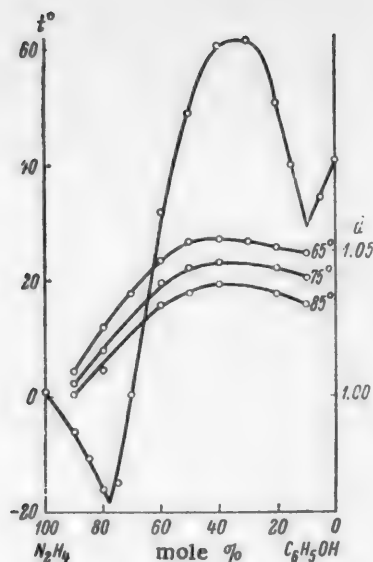
Fig. 1. Fusion diagram and density (d) of the system hydrazine-phenol.
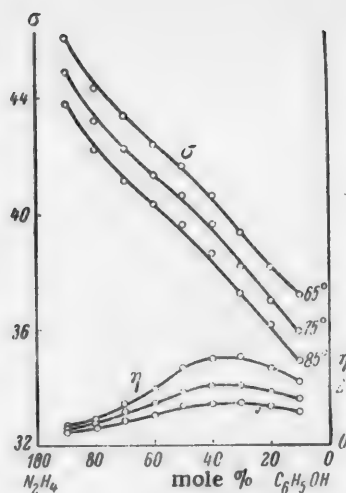
Fig. 2. Surface tension (σ) and viscosity (η) in the system hydrazine-phenol.
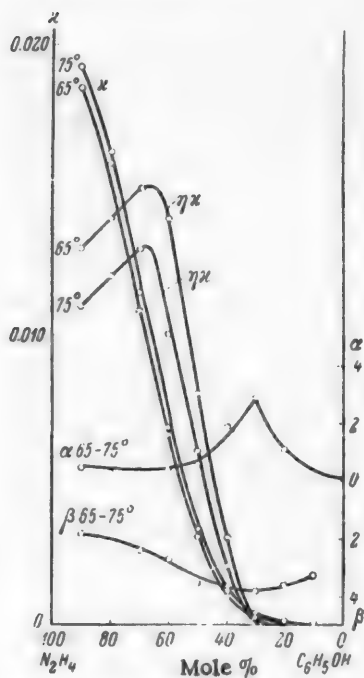
Fig. 3. Specific electroconductance (κ), corrected electroconductance (ηκ), and temperature coefficients of electroconductance (α) and viscosity (β) in the system hydrazine—phenol.

TABLE 1

Fusion in the System Hydrazine-Phenol

Amount of phenol in mixture (mole %)	Melting point	Amount of phenol in mixture (mole %)	Melting point
10.0	− 6.0°	50.0	+49.0°
14.9	−10.0	60.0	60.0
20.0	−16.0	70.0	61.5
24.9	−15.0	80.0	50.5
30.0	+ 0.0	90.0	29.0
40.0	+32.0	95.0	34.0

The surface tension curves (Table 2, Fig. 2) have an S-like shape, and drop quite sharply in going from hydrazine to phenol.

The results of measuring the viscosity are given in Table 2 and plotted in Fig. 2. The viscosity isotherms have a maximum, corresponding to the compound $N_2H_4 \cdot 2C_6H_5OH$.

The results of measuring the specific electroconductance are given in Table 3 and plotted in Fig. 3. The electroconductance decreases rapidly in going from pure hydrazine to 33% phenol, and then the decrease is more gentle in going on to pure phenol.

TABLE 2

Density (d), Surface Tension (σ) and Viscosity (η) in the System Hydrazine-Phenol

Amount of phenol (mole %)	d			σ			η		
	65°	75°	85°	65°	75°	85°	65°	75°	85°
10.0	1.009	1.005	1.001	46.98	44.93	43.81	0.711	0.588	0.493
20.0	1.024	1.016	1.009	44.35	43.21	42.27	0.909	0.752	0.633
30.0	1.035	1.027	1.021	43.40	42.24	41.09	1.454	1.126	0.889
40.0	1.047	1.039	1.031	42.38	41.30	40.35	1.909	1.441	1.093
50.0	1.053	1.044	1.035	41.64	40.62	39.60	2.636	1.832	1.360
60.0	1.054	1.046	1.039	40.61	39.60	38.55	2.973	2.036	1.467
70.0	1.053	1.046	1.037	39.37	38.10	37.24	3.049	2.078	1.472
80.0	1.051	1.044	1.035	38.18	36.98	36.15	2.629	1.823	1.310
90.0	1.049	1.040	1.031	37.24	35.88	34.88	2.149	1.540	1.177

DISCUSSION OF RESULTS

The presence of a maximum on both the density and viscosity isotherms indicates the formation and existence of a compound in the homogeneous melt found in the system hydrazine—phenol. A considerable smoothing out of the maximum on the viscosity isotherms occurs when the temperature is raised from 65 to 85°, which is due to decomposition of the compound. The S-like shape of the surface tension isotherms also indicates the existence of the compound $N_2H_4 \cdot 2C_6H_5OH$. The electroconductance isotherms show a sharp change in the slope with respect to the composition axis, which can be attributed to the compound $N_2H_4 \cdot 2C_6H_5OH$. To allow for the influence of viscosity on the electroconductance, we multiplied these values together (Table 3, Fig. 3). From Fig. 3

TABLE 3

Specific Electroconductance (κ), Corrected Electroconductance ($\eta\kappa$), and Temperature Coefficients of Electroconductance (α) and Viscosity (β) in the System Hydrazine—Phenol

Amount of phenol (mole %)	κ		$\eta\kappa$		α	β
	65°	75°	65°	75°	65—75°	65—85°
10.0	0.0184	0.0192	0.013	0.011	0.425	−1.894
20.0	0.0159	0.0163	0.014	0.012	0.249	−1.890
30.0	0.0108	0.0114	0.015	0.013	0.540	−2.543
40.0	0.0066	0.0068	0.013	0.010	0.298	−2.794
50.0	0.0030	0.0032	0.008	0.006	0.625	−3.599
60.0	0.0010	0.0012	0.003	0.002	1.818	−3.741
70.0	0.0003	0.0004	0.009	0.008	2.857	−3.787
80.0	0.00009	0.0001	0.002	0.0001	1.0	−3.621
90.0	0.00001	0.00001	0.0002	0.00001	—	−3.302

it can be seen that the corrected electroconductance isotherms rise in going from pure hydrazine to 30% phenol, and then their change is similar to that of the specific electroconductance isotherms. We also calculated the temperature coefficients of the electroconductance using the equation

$$\iota = \frac{1}{\varkappa_{av}} \cdot \frac{\varkappa_2 - \varkappa_1}{t_2 - t_1} \cdot 100.$$

The data for the curves of the temperature coefficients of the electroconductance (α) are given in Table 3 and plotted in Fig. 3. The curves show a maximum, corresponding to the compound $N_2H_4 \cdot 2C_6H_5OH$.

A similar equation was used to calculate the temperature coefficients of the viscosity (β) (Table 3); since these values are negative, they were plotted below the line for the zero values of this property. The curves for the temperature coefficients of the viscosity (Fig. 3) show a minimum corresponding to the 1:2 compound.

As a result, all of the properties studied by us indicate the existence of a compound of hydrazine with phenol, both in the solid phase and in the homogeneous melt.

Assuming that the indicated compound is formed along the lines of hydrogen bonding, it then becomes possible to assign the following hypothetical structure to it.
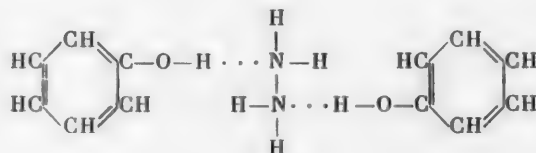
SUMMARY

1. The fusion diagram of the system hydrazine—phenol was investigated. It was established that the compound $N_2H_4 \cdot 2C_6H_5OH$ exists in the solid phase.

2. The density, viscosity, surface tension, and specific electroconductance in the system were investigated. The isotherms of these properties revealed that the indicated compound also exists in the homogeneous melt. Maxima were observed on the isotherms of both the density and the viscosity. The surface tension isotherms have an S-like shape, while the specific electroconductance isotherms show a sharp change in the slope, corresponding to the indicated compound.

3. The curves for the temperature coefficients of both the electroconductance and the viscosity confirm the presence of a compound with a 1:2 ratio of the components. Here the electroconductance curves show a maximum, and the viscosity curves show a minimum.

4. Proceeding from the concepts of hydrogen bonding, a scheme was given for the formation of compounds between hydrazine and phenol.

LITERATURE CITED

[1] G. Brauer, Manual on Preparative Inorganic Chemistry [Russian translation] (IL, 1956).

[2] P. A. Rebinder, J. Exptl. Biology and Medicine [USSR] 4, 99 (1927).

POLAROGRAPHY OF SOME AROMATIC MONONITRO COMPOUNDS

V. M. Gorokhovskii and N. M. Ponomareva

Kazan Branch of the All-Union Motion Picture Scientific Research Institute

The nature and position of substituents in the benzene ring exert considerable influence on the ability of the nitro group to be reduced at the dropping mercury electrode. For all nitro compounds, both the half-wave potential and the value of the diffusion current depend on the pH of the solution. The pH and the composition of both the solvent and the support also exert a definite influence on the mechanism involved in the reduction of the nitro group. Although a relatively large number of papers exists in the literature on the polarography of individual aromatic nitro compounds [1, 2], still the investigation results of the different authors can be compared only with difficulty due to the different experimental conditions used. A systematic study on the polarography of nitrobenzene, o-, m- and p-nitrophenols, the nitroanisoles, and the nitrobenzoic acids and their methyl esters, at different pH and concentrations, was made by Page and co-workers[3]. The influence exerted by the nature of the substituents on the ability of the nitro group to reduce was investigated.

Data is lacking in the literature on the relative influence exerted by two different substituents in the benzene ring on the ability of the nitro group to reduce. The purpose of the present investigation was to study the reduction of 4-nitrosalicylic and 5-nitroanthranilic acids, and also of o- and p-nitrobenzoic acids and of p-nitroaniline, at the dropping mercury electrode.

EXPERIMENTAL

A visual polarographic setup, assembled in conventional manner, was used to take the polarograms. To measure the current strength we sued a B-27 mirror galvanometer, having an operating sensitivity of 7.5×10^{-2} μ amp/mm. The characteristic of the capillary was $m^{2/3} t^{1/6} = 1.66 \, mg^{2/3} \cdot sec^{-1/2}$. All of the measurements were run in a thermostat at $25 \pm 0.5°$. A stream of hydrogen was passed through the investigated solution for 10 min to remove dissolved oxygen. A saturated calomel electrode was used as the anode. The pH of the solutions was measured using an LP-5 bulb pH meter.

The purity of the investigated compounds was verified by comparing their melting points with those given in the literature [4] (in parentheses): o- and p-nitrobenzoic acids 145—147° (148°) and 238—239° (238°), respectively; p-nitroaniline 147.5° (147.5°); 4-nitrosalicylic acid 228—230° (228—230°); 5-nitroanthranilic acid 272—275° (260—280). As buffer solutions we used acetate, phthalate, phosphate, and borate mixtures [5, 6], prepared from either c. p. or pharmaceutical grade chemicals. The original solutions of the investigated nitro derivatives were prepared by the exact weighing of the compounds in 96% alcohol.
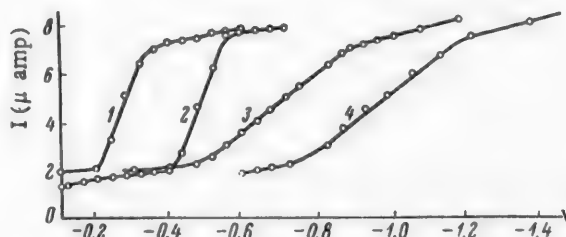
Fig. 1. Polarograms of o-nitrobenzoic acid in buffer solutions containing 4.8% C_2H_5OH and 0.01% agar-agar.

pH: 1) 2.4, 2) 5.3; 3) 7.9; 4) 9.6.
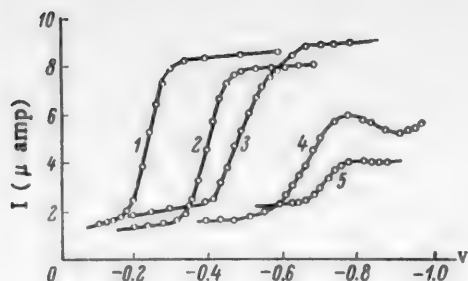
Fig. 2. Polarograms of p-nitrobenzoic acid in buffer solutions, containing 4.8% C_2H_5OH and 0.01% agar-agar.

pH: 1) 3.1, 2) 5.3, 3) 6.2, 4) 8.0, 5) 10.2.

Nitrobenzoic Acids

The half-wave potential $E_{1/2}$ as a function of the pH was studied using 5×10^{-4} molar solutions of o- and p-nitrobenzoic acids (Figs. 1 and 2). Changing the pH from 1.5 to 10 causes $E_{1/2}$ to shift toward negative potentials. In some cases the appearance of an ill-defined, more negative second wave is observed. In the pH range studied, the slope coefficient of the wave   for o- and p-nitrobenzoic acids changes from 0.07 to 0.2 and from 0.05 to 0.1, respectively, which is apparently associated with a change in the mechanism of the reduction. For both isomeric acids, the value of the diffusion current in the pH range from 2 to 6 lies within 6—6.5 μamp, but when the pH is increased further the diffusion current in the case of o-nitrobenzoic acid drops to 5—5.5 μamp, while the height of the wave in the case of p-nitrobenzoic acid decreases to 2—3 μamp. The plots showing the relationship between $E_{1/2}$ and the pH for the o- and p-nitrobenzoic acids are straight lines with slope tangents α 0.088 and 0.074, respectively.
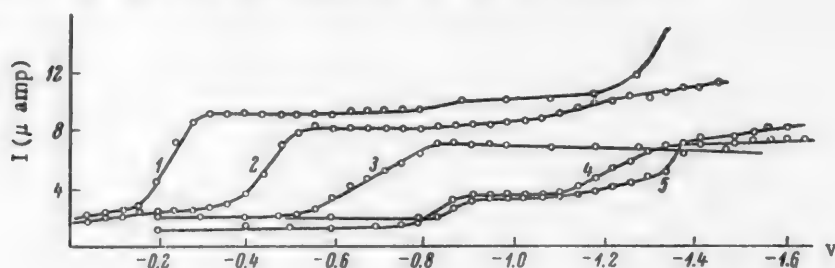
Fig. 3. Polarograms of 4-nitrosalicylic acid (4×10^{-4}M) in buffer solutions containing 9.6% C_2H_5OH and 0.004% agar-agar.

pH: 1) 2.1, 2) 4.0, 3) 6.4, 4) 8.7, 5) 9.8.

TABLE 1

Influence on pH on the Reduction of 4-Nitrosalicylic Acid (4×10^{-4}M) in Buffer Solutions Containing 9.6% Alcohol and 0.004% Agar-Agar

pH	I_{total} (μ amp)	Wave I		Wave II	
		i_1 (μa)	$E_{1/2}$ (V)	i_2 (μa)	$E_{1/2}$ (V)
2.1	6.75	6.75	0.22	—	—
4.0	9.3	5.4	0.43	3.9	1.27
5.2	4.95	4.95	0.53	—	—
5.8	4.8	4.8	0.61	—	—
6.4	5.1	5.1	0.65	—	—
7.5	4.2	3.0	0.78	1.2	1.35
8.3	5.1	2.1	0.81	3.0	1.40
9.4	5.7	1.65	0.82	4.05	1.34
9.8	5.4	0.9	0.85	4.5	1.31
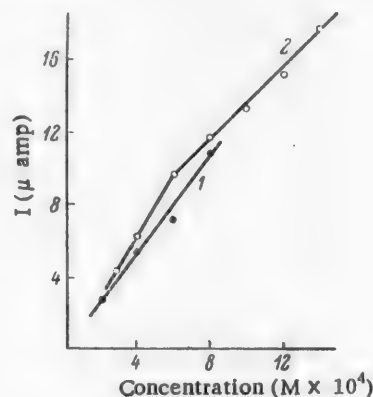
Fig. 4. Value of the diffusion current as a function of concentration. 1) for 4-nitrosalicylic acid at pH 4.0, 2) for 5-nitroanthranilic acid at pH 4.6.

TABLE 2

Effect of Alcohol on the Reduction of 5-Nitroanthranilic Acid
$(2 \times 10^{-4}M)$ in Buffer Solutions

C_2H_5OH (in %)	pH	I_{total} (μ amp)	Wave I		Wave II	
			i_1 (μ.a)	E_1 (v)	i_2 (μ.a)	$E_{1/2}$ (v)
9.6	4.4	6.75	1.8	0.16	4.95	0.40
19.2	4.4	7.5	2.7	0.14	4.8	0.44
28.8	4.2	8.1	3.6	0.18	4.5	0.52
38.4	4.4	7.0	2.3	0.17	4.65	0.55
48.0	4.6	8.7	5.25	0.18	3.45	0.66

4-Nitrosalicylic Acid

The reduction of 4-nitrosalicylic acid at the dropping mercury electrode was studied in the pH range from 2 to 10 (Fig. 3). The polarograms of the nitrosalicylic acid in the region $4 > pH > 7.5$ consist of two waves. When the pH is changed from 2 to 10, $E_{1/2}$ of the first wave shows a steady shift toward negative potentials (Table 1). $E_{1/2}$ of the second wave remains practically constant in this pH range, staying within the limits 1.3—1.4 v; in the pH region < 4 it apparently merges with the hydrogen wave of the support. In the pH region > 7.5 the first wave decreases, while the second wave increases.
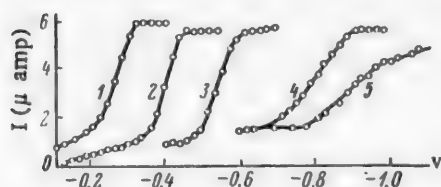
Fig. 5. Polarograms of 5-nitroanthranilic acid $(2 \times 10^{-4}M)$ in buffer solutions, containing 2% C_2H_5OH and 0.004% agar-agar.

pH: 1) 2.3, 2) 4.0, 3) 5.9, 4) 8.3, 5) 10.1.

The heights of both waves of 4-nitrosalicylic acid increase with increase in the concentration of the acid. When the 4-nitrosalicylic acid concentration is changed from 2×10^{-3} to $8 \times 10^{-3}M$, the first wave obeys the equation $i = kc$ (Fig. 4). The slope coefficient of the first wave in the pH range from 2 to 10 changes from 0.04 to 0.09. For the second wave it is 0.1—0.15.

5-Nitroanthranilic Acid

The reduction of 5-nitroanthranilic acid was investigated in pH range from 2 to 10 (Fig. 5.). The height of the 5-nitroanthranilic acid wave in this pH range changes from 5 to 2.7 μamp, while $E_{1/2}$ shifts toward negative potentials. The slope coefficient in the pH range from 2 to 10 changes from 0.04 to 0.1. The plot of $E_{1/2}$ versus pH is a straight line with tan $\alpha = 0.079$.

The plot of the value of the diffusion current as a function of the 5-nitroanthranilic acid concentration is shown in Fig. 4. We investigated the effect of the alcohol concentration on the polarographic characteristics of 5-nitroanthranilic acid (Table 2). Two waves appear on the polarogram of 5-nitroanthranilic acid when the alcohol concentration is increased. $E_{1/2}$ of the first wave remains practically constant when the alcohol concentration is increased, staying within the limits 0.15—0.2 v; $E_{1/2}$ of the second wave shifts toward negative potentials in proportion to the increase in the alcohol concentration.

p-Nitroaniline

The reduction of p-nitroaniline $(5 \times 10^{-4}M)$ in buffer solutions containing 10% C_2H_5OH, was studied in the pH range from 1.4 to 11.4 (Fig. 6). In all cases the polarogram consisted of one wave, the $E_{1/2}$ of which showed steady shift toward negative potentials as the pH was increased. The slope coefficient of the wave lay between 0.03 and 0.08. The height of the wave in the pH range from 1.4 to 8 was 5.8—5.2 μamp, and at pH > 8 it decreased to 3.5—4 μamp.

As had been done earlier [3], to compare the ability of the nitro compounds studied by us to reduce, we will take $E_{1/2}$ of nitrobenzene as the standard. As had been established for nitrobenzene [3], and also by us for 5-nitroanthranilic acid (Table 2), $E_{1/2}$ of nitro compounds shifts toward the negative side on the average of 5 mv per 1% increase in the alcohol concentration. Consequently, to convert the results to the same conditions, all of the $E_{1/2}$ values of the nitro compounds were recalculated, assuming that the investigated solution contains 10% alcohol. The plots characterizing the ability of the different nitro compounds to reduce are shown in Figs. 7 and 8. The zero line

Fig. 6. Polarograms of p-nitroaniline (5×10^{-4}M) in buffer solutions containing 10% C_2H_5OH and 0.01% agar-agar.

pH: 1) 1.4, 2) 3.6, 3) 6.5, 4) 8.7, 5) 11.4.

corresponds to $E_{1/2}$ of nitrobenzene. • The difference, ΔE, between $E_{1/2}$ of a given nitro compound and $E_{1/2}$ of nitrobenzene, is plotted along the ordinates. In such case a decrease in the value of ΔE will be linked with a shift of $E_{1/2}$ toward negative values of the potential, and consequently, with a decrease in the ability of the nitro compound to reduce. In this respect it is interesting to compare 4-nitrosalicylic acid with p-nitrobenzoic acid and n-nitrophenol • (Fig. 7).
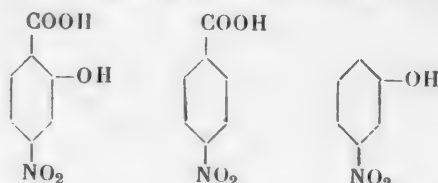
The ability of the nitro group in p-nitrobenzoic acid to be reduced decreases monotonically with increase in the pH (Fig. 7). In the pH region < 9 the electronegative p-carboxyl group facilitates reduction of the nitro group. The reduction of the nitro group becomes difficult at high pH values, apparently due to the influence exerted by the negative charge of the dissociated carboxyl group [3].
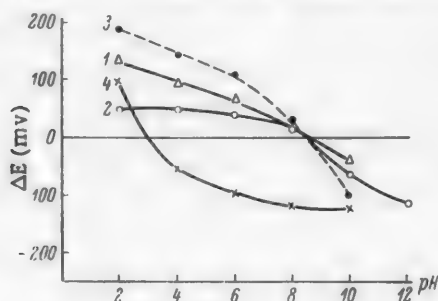
Fig. 7. Influence of pH on the ability to be reduced: difference in half-wave potentials (ΔE) of given nitro compound and nitrobenzene as a function of pH.

1) for p-nitrobenzoic acid, 2) m-nitrophenol, 3) sum of ΔE for p-nitrobenzoic acid and m-nitrophenol, and 4) for 4-nitrosalicylic acid.

Fig. 8. Influence of pH on the ability to be reduced.

1) for m-nitrobenzoic acid, 2) for p-nitroaniline, 3) sum of ΔE for m-nitrobenzoic acid and p-nitroaniline and 4) for 5-nitroanthranilic acid.

A similar effect, but less weakly expressed, is shown by the hydroxyl group in m-nitrophenol (Fig. 7). The electropositive OH group in m-nitrophenol, substantially increasing the electron density in the o- and p- positions, decreases the electron density in the m- position, and in this manner facilitates reduction of the nitro group.

• From the data in [3].

Assuming the absence of a mutual effect exerted by the groups, the total effect of the COOH and OH groups in 4-nitrosalicylic acid should lead to an even greater reduction in the electronegativity of the nitro group (shown by the broken line in Fig. 7), and consequently, to an increase in the ability to be reduced. However, as was found experimentally, the electronegativity of the nitro group in 4-nitrosalicylic acid shows substantial increase: at pH < 3, 4-nitrosalicylic acid is reduced more easily than nitrobenzene, while at pH > 3 the electronegativity of the nitro group shows substantial increase (Fig. 7). It is interesting to mention that at extreme values, pH< 2 or > 10, Curves 3 and 4 in Fig. 7 approach each other. In this case, the mutual influence of the COOH and OH groups is apparently slight, and the total ΔE effect of p-nitrobenzoic acid and m-nitrophenol is close to the ΔE of 4-nitrosalicylic acid.

The ability of 5-nitroanthranilic acid to be reduced can be compared to that shown by m-nitrobenzoic acid [*] and p-nitroaniline.

$$\text{HOOC-}\underset{NO_2}{\overset{NH_2}{\bigcirc}} \qquad \text{HOOC-}\underset{NO_2}{\overset{NH_2}{\bigcirc}} \qquad \underset{NO_2}{\overset{NH_2}{\bigcirc}}$$
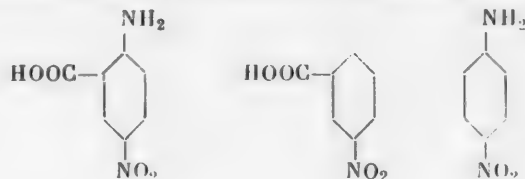
At pH < 6, the ease with which m-nitrobenzoic acid is reduced is greater than that shown by nitrobenzene, since a carboxyl group in the m- position favors increasing the electron density in the o- and p- positions and reduces somewhat the electron density around the m-nitro group. At pH > 6, the negative charge of the carboxyl will favor increasing the electron density around the nitro group. The electronegativity of the NO_2 group, as was shown in [3] and confirmed by us, increases as the distance between the COOH and NO_2 groups in a molecule decreases, i.e., in the order o > m > p. The electronegativity of the nitro group in p-nitroaniline is somewhat greater than it is in nitrobenzene, due to the electron-donor influence of the amino group. The ability of the nitro group in p-nitroaniline to be reduced is practically independent of the pH (Fig. 8). Excluding the mutual influence of the COOH and NH_2 groups, ΔE of 5-nitroanthranilic acid can be depicted by Curve 3 in Fig. 8. The experimental value of ΔE for 5-nitroanthranilic acid (Curve 4) is quite close to the theoretical value. Curves 3 and 4 are especially close to each other at pH < 6, where the visible effect of the mutual influence of the COOH and NH_2 groups is expressed weakly. At pH > 6, the mutual influence of the COOH and NH_2 groups appears more strongly and the curves separate.

Summarizing the above, it is possible to assume that the polarographic method permits obtaining some quantitative date regarding the mutual influence exerted by different substituents in the benzene ring.

SUMMARY

1. The reduction of o- and p-nitrobenzoic acids, 4-nitrosalicylic acid, 5-nitroanthranilic acid,and p-nitroaniline at the dropping mercury electrode, in the pH range from 2 to 10, was studied.

2. Reasons were given why the polarographic method permits obtaining a quantitative estimate as to the mutual influence exerted by different substituents in the benzene ring.

LITERATURE CITED

[1] A. P. Terent'ev and L. A. Yanovskaya, "The polarographic method in organic chemistry". Collection: Reactions and Methods of Study of Organic Compounds [in Russian] (Goskhimizdat, Moscow, 1957), Vol. 5

[2] K. Schwabe. Polarographie und chemische Konstitution organischer Verbindungen. (Berlin, 1957).

[3] J. E. Page, J. W. Smith,and J..G. Waller, J. Phys. and Colloid Chem. 53, 545 (1949).

[4] F. K. Beilstein. Handbuch der organischen Chemie. (Berlin,.1928—1941).

[5] Yu. Yu. Lur'e, Calculation and Reference Tables for Chemists [in Russian] (Goskhimizdat, 1947).

[6] E. N. Vinogradova, Methods for Determining Hydrogen-Ion Concentration [in Russian] (Izd. MGU, 1956).

*From the data in [3].

CYCLOPROPANES AND CYCLOBUTANES

VII. TOLYL- AND ANISYLCYCLOBUTANES

R. Ya. Levina, Yu. S. Shabarov, M. G. Kuz'min,

N. I. Vasil'ev, S. I. Pokraka, and E. G. Treshchova

Moscow State University

In previous communications [1, 2] we described a new method for the synthesis of arylcyclobutanes, consisting in the catalytic decomposition of aryltetrahydropyridazines; using this reaction, we synthesized the phenyl- and p-tolycyclobutanes, and also 1, 2-diphenylcyclobutane. In this paper we describe the synthesis, using the same method, of all of the isomeric tolylcyclobutanes, and also of o- and p-anisylcyclobutanes.

The starting aryltetrahydropyridazines (II) were easily obtained from 1, 2-dicarbethoxy-3-aryltetrahydropyridazines (I) the adducts of the corresponding arylbutadienes (isomeric tolyl- and anisylbutadienes)* with the diethyl ester of azodicarboxylic acid — by the hydrolysis of these adducts (alcoholic caustic), going with simultaneous decarboxylation and shift of the double bond to the nitrogen [4].
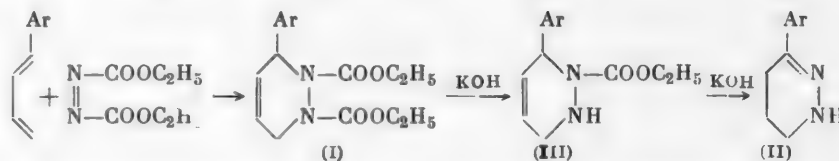
The 3-aryltetrahydropyridazines (II) obtained in this manner were characterized by reacting them with phenyl isothiocyanate to give the corresponding phenylthiourea derivatives (anilides of the corresponding thiocarboxylic acids), analysis of which revealed that only one molecule of phenyl isothiocyanate enters into the reaction, and consequently the obtained aryltetrahydropyridazines contain only one NH group (i.e., the double bond is found between carbon and nitrogen, in the 2, 3 position). It was also established (on two examples, where aryl = o- and p-tolyl) that the hydrolysis of adducts (I) under milder conditions permits isolating the intermediate hydrolysis product, namely, 2-carbethoxy-3-aryltetrahydropyridazine (III), which reacts with phenyl isothiocyanate to give the anilide of the corresponding thiocarboxylic acid; the ability to react in this manner, testifying to the presence

---

*The tolylbutadienes were synthesized by the chloroarylation of butadiene with the proper tolyldiazonium salts in the presence of cupric chloride and subsequent dehydrochlorination of the obtained chlorobutenes [3].

$$CH_2=CH-CH=CH_2 + CH_3C_6H_4N_2Cl \xrightarrow{CuCl_2} CH_3C_6H_4-CH_2-CH=CH-CH_2Cl \xrightarrow{KOH}$$
$$\rightarrow CH_3C_6H_4-CH=CH-CH=CH_2$$
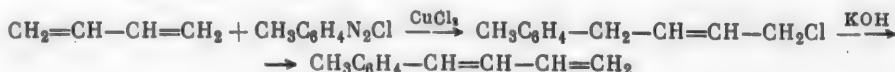
The o- and p-anisylbutadienes were synthesized by a different, more convenient procedure, namely, by the dehydration of the alcohols obtained by Grignard synthesis from o- and p-methoxybenzaldehydes and allyl chloride.

$$CH_3OC_6H_4CHO + Mg + CH_2=CH-CH_2Cl \rightarrow CH_3OC_6H_4CHOHCH_2CH=CH_2 \xrightarrow{KHSO_4}$$
$$\rightarrow CH_3OC_6H_4CH=CH-CH=CH_2$$
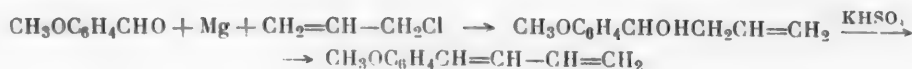
of an NH group in the product of the partial hydrolysis of adducts (I), permits postulating that it is the carbethoxyl group, furthest removed from the aryl group, that suffers hydrolysis and decarboxylation first. •

The 3-aryltetrahydropyridazines (II) were decomposed by heating them in the presence of KOH and platinum; the intermediate biradical (IV), formed with the evolution of nitrogen, then suffered conversion to the arylcyclobutane (V), and also suffered cleavage with the formation of the corresponding styrene and ethylene [1, 2].

$$(II) \xrightarrow{KOH,\ Pt} \left[\begin{array}{c} Ar \\ \\ N \\ \\ N \end{array} \right] \xrightarrow{-N_2} \left[\begin{array}{c} Ar \\ \bullet \\ \\ \bullet \end{array} \right] \begin{array}{c} Ar-\square\ (V) \\ \\ ArCH=CH_2 + CH_2=CH_2 \end{array}$$

(IV)
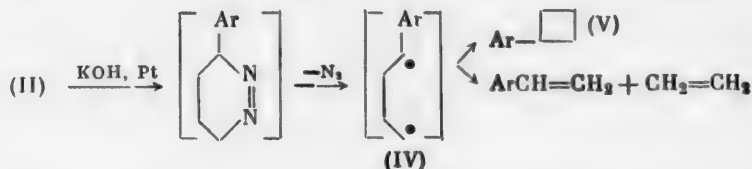
The obtained arylcyclobutanes were easily purified from the lower boiling styrenes by fractional distillation through a column, after which they contained, judging from the Raman spectra, only traces of unsaturated compounds (except o-tolylcyclobutane, which was purified further by treatment with 2, 4-dinitrophenylsulfenyl chloride [5], and then fractionated again through a column). The arylcyclobutanes were also characterized by their ultraviolet absorption spectra (an SF-4 spectrophotometer was used to take the spectra). • • The UV absorption spectra of all of the isomeric tolylcyclobutanes are shown in Fig. 1, while those of the o- and p-anisylcyclobutanes are shown in Fig. 2. For comparison, we give in Fig. 3 the spectra of phenylcyclobutane and 1, 2-diphenylcyclobutane (mixture of stereoisomers), the synthesis of which had been described by us earlier [1, 2].

From the presented spectra it can be seen that the arylcyclobutanes studied by us have, in the main, a characteristic absorption minimum in the wave length region $230-240$ m μ, and a characteristic maximum in the $260-270$ mμ region. The absorption curve of phenylcyclobutane shows a maximum in the 260 mμ region, but the corresponding minimum is apparently shifted toward shorter wavelengths ($220-230$ m μ), and is found outside the resolving ability of the instrument.

It should be mentioned that the UV absorption spectra of the arylcyclobutanes and corresponding arylcyclopropanes have a similar character, and differ substantially from the spectra of the corresponding styrenes. The latter show more intense absorption, with a maximum in the 255 mμ region. Below, in Fig. 4, we give for comparison the UV absorption spectra of p-propenyltoluene, p-tolylcyclopropane and p-tolylcyclobutane, and in Fig. 5, the spectra of p-propenylanisole, p-anisylcyclopropane and p-anisylcyclobutane.

EXPERIMENTAL

o-, m- and p-Tolyl-1, 3-butadienes. The chloroarylation of butadiene with the proper tolyldiazonium chloride was run in the presence of cupric chloride and calcium oxide [3]. The yield of the isomeric 4-chloro-1-tolyl-2-butenes was $50-55\%$.

Fig. 1.

1 — o-tolylcyclobutane
(λ_{min} 235 mμ, log ϵ_{min} 2.04;
λ_{max} 264 mμ, log ϵ_{max} 2.45;
λ_{min} 270 mμ, log ϵ_{min} 2.29;
λ_{max} 272 mμ. log ϵ_{max} 2.33);
2 — m-tolylcyclobutane
(λ_{min} 235 mμ, log ϵ_{min} 1.81;
λ_{max} 266 mμ, log ϵ_{max} 2.29;
λ_{min} 270 mμ, log ϵ_{min} 2.12;
λ_{max} 272 mμ. log ϵ_{max} 2.13);
3 — p-tolylcyclobutane
(λ_{min} 238 mμ, log ϵ_{min} 2.21;
λ_{max} 260 mμ, log ϵ_{min} 2.66;
λ_{min} 264 mμ, log ϵ_{min} 2.64;
λ_{max} 266 mμ. log ϵ_{max} 2.71;
λ_{min} 272 mμ, logϵ_{min} 2.61;
λ_{max} 275 mμ. logϵ_{max} 2.68).

• In the opposite case the double bond should shift to the 2, 3 position, and the presence of a free NH group could not be shown.

• •We wish to thank L. A. Kazitsyna for taking the ultraviolet absorption spectra.

Fig. 2.

1 — o-Anisylcyclobutane (λ_{min} 240 mμ, logϵ_{min} 2.51; λ_{max} 272 mμ, logϵ_{max} 3.33; λ_{min} 276 mμ, logϵ_{min} 3.24; λ_{max} 278 mμ, logϵ_{max} 3.34; λ_{min} 296 mμ, logϵ_{min} 1.95; λ_{max} 298 mμ, log ϵ_{max} 1.99). 2 — p-Anisylcyclobutane (λ_{max} 228 mμ, logϵ_{max} 4.56; λ_{min} 245 mμ, logϵ_{min} 2.22; λ_{max} 279 mμ, logϵ_{max} 3.42; λ_{min} 283 mμ, ϵ_{min} 3.16; λ_{max} 286 mμ, logϵ_{max} 3.39).

Fig. 3.

1 — Phenylcyclobutane (λ_{max} 255 mμ, logϵ_{max} 2.64; λ_{min} 258 mμ, log ϵ_{min} 2.60; λ_{max} 260 mμ; logϵ_{max} 2.61); 2 — 1, 2- Diphenylcyclobutane(λ_{min} 246 mμ, logϵ_{min} 2.33; λ_{max} 262 mμ, log ϵ_{min} 2.61; λ_{min} 268 mμ, logϵ_{min} 2.44; λ_{max} 269 mμ, log ϵ_{max} 2.47).

Fig. 4.

1 — p-Propenyltoluene (λ_{max} 253 mμ, logϵ_{max} 4.103; λ_{min} 284 mμ, logϵ_{min} 2.844; λ_{max} 287 mμ, logϵ_{max} 2.875; λ_{min} 295 mμ, logϵ_{min} 2.589; λ_{max} 297 mμ, logϵ_{max} 2.671); 2 — p-Tolylcyclopropane (λ_{min} 240 mμ, log ϵ_{min} 3.164; λ_{max} 255 mμ, logϵ_{max} 3.330; λ_{min} 277 mμ, logϵ_{min} 2.611; λ_{max} 280 mμ, log ϵ_{max} 2.778; λ_{min} 295 mμ, log ϵ_{min} 1.741; λ_{max} 298 mμ, logϵ_{max} 1.878). 3 — p-Tolylcyclobutane (see Fig. 1).
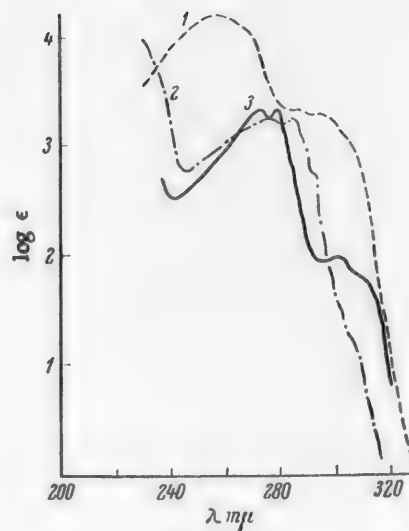
Fig. 5.

1 — p-Propenylanisole (λ_{max} 258 mμ, logϵ_{max} 4.245) 2 — p-Anisylcyclopropane (λ_{max} 229 mμ, logϵ_{max} 4.127; λ_{min} 248 mμ, logϵ_{min} 2.982; λ_{max} 278 mμ, log ϵ_{max} 3.255); 3 — p-Anisylcyclobutane (see Fig. 2).

TABLE 1
3-Aryl-1,2-dicarbethoxy-1,2,3,6-tetrahydropyridazines (I)

Aryl	Yield %	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR$_D$ found	MR$_D$ calc.	EM$_D$	Found % C	Found % H	Found % N	Calculated % C	Calculated % H	Calculated % N
o-Tolyl	80	199—200°(11)	1.5215	1.1398	85.12	84.90	0.22	64.03, 64.19	7.12, 7.04	9.03, 8.93	64.13		8.80
m-Tolyl	88	194—195 (8)	M.p. 58—58.5° (from petroleum ether)							8.61, 8.81		6.97	8.80
p-Tolyl	90	175—176 (2.5)	1.5195	1.1266	85.84	84.90	0.94			9.06, 8.86			8.80
o-Anisyl	88	215—216 (12)	1.5280	1.1796	87.25	86.54	0.71			8.25, 8.43			8.38
p-Anisyl	85	198—199 (4)	M.p.65—66°** 1.5265	1.1738	87.47	86.54	0.93	61.07, 61.05	6.77, 6.63	—	61.06	6.63	—

* The atomic refraction of nitrogen was taken equal to 2.48 [8].
** Crystallized after standing for 2 weeks at 40°.

4-Chloro-1-o-tolyl-2-butene: b. p. 115—117 (11 mm) n_D^{20} 1.5391; 4-chloro-1-m-tolyl-2-butene: b. p. 119—121° (9 mm), n_D^{20} 1.5347; 4-chloro-1-p-tolyl-2-butene: b. p. 121—123 (10 mm), n_D^{20} 1.5345. Literature [3]: for the o-isomer: b.p. 94—95° (2 mm), n_D^{20} 1.5400; m-isomer: b.p. 107—109° (3 mm), n_D^{20} 1.5354; p-isomer: b.p. 112—114° (6 mm), n_D^{20} 1.5349.

Dehydrochlorination of the chlorotolylbutenes [3] gave the isomeric 1-tolyl-1,3-butadienes in 85—90% yield.

1-o-Tolyl-1,3-butadiene: b.p. 99—101° (15 mm), n_D^{20} 1.5989; 1-m-tolyl-1,3-butadiene: b.p. 97—98° (13 mm) n_D^{20} 1.5978; 1-p-tolyl-1,3-butadiene: b.p. 94—95° (11 mm) m.p. 24—25°. Literature [3]: for the o-isomer: b.p. 86° (8 mm), n_D^{20} 1.6001; m-isomer: b.p. 85—87° (7 mm), n_D^{20} 1.5995; p-isomer: b.p. 90—91° (9 mm), m.p. 26°.

o- and p-Anisyl-1,3-butadienes. Allyl chloride (5 ml) was added with stirring to 26 g of magnesium in 250 ml of absolute ether, and then a solution composed of 236 g of the proper methoxybenzaldehyde * and 85 g of allyl chloride in 400 ml of absolute ether was gradually added at such a rate that the reaction mixture refluxed vigorously. The stirring was continued for 3 hr at room temperature; then the reaction mixture was poured on a mixture of ice and ammonium chloride. After working up the ether extracts in the usual manner, followed by removal of the ether by distillation, the residue (in 60 g portions) was heated on the water bath with freshly dehydrated potassium bisulfate (5 g) for 10 min in a nitrogen stream, and then rapidly vacum-distilled. The distillate was dried over calcium chloride, and the obtained anisylbutadiene was again redistilled in vacuo (in a stream of nitrogen).

1-o-Anisyl-1,3-butadiene (60% yield): b.p. 140—143° (16 mm), n_D^{20} 1.6140; 1-p-anisyl-1,3-butadiene (70% yield): b.p. 139—140° (12 mm) m.p. 44—45°. Corresponding literature data: b.p. 68° (0.05 mm), n_D^{20} 1.6169 [7]; b.p. 115—120° (6 mm) m.p. 45° [3].

The adducts (I) of the diethyl ester of azodicarboxylic acid with 1-aryl-1,3-butadienes were obtained by pouring together solutions composed of equimolar amounts of the reactants in an equal volume of anhydrous benzene with cooling (0—5°); the reaction mixture was allowed to stand overnight at room temperature. The solvent was distilled off, and the residue was vacum distilled to yield the adducts, the constants of which are given in Table 1.

3-Aryl-1,4,5,6-tetrahydropyridazines (II). A solution of 3.0 moles (168 g) of KOH in 600 ml of alcohol

---

* o-Methoxybenzaldehyde [b.p. 165-166° (14 mm) n_D^{20} 1.5612] was obtained in 72% yield by the methylation of salicylaldehyde with dimethyl sulfate [6].

TABLE 2

3-Aryl-1,4,5,6-tetrahydropyridazines (II)

Aryl	Yield (in %)	Boiling point (pressure in mm)	Melting point (from petroleum ether)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated[*]	EM_D	Phenylthiourea melting point	Phenylthiourea found N(%)	Phenylthiourea calculated N(%)
o-Tolyl ..	75	154—155° (9)	—	1.5847	1.0667	54.72	54.27	0.45	—	—	—
m-Tolyl ..	80	164—164.5 (8)	38°	—	—	—	—	—	122.5—123°	13.71, 13.56	13.58
p-Tolyl ..	85	171—172 (12)	80	—	—	—	—	—	—	—	—
o-Anisyl .	89	178—180 (12)	—	1.5880	1.1307	56.62	55.53	1.09	141—142	14.13 14.33	14.40
p-Anisyl**	82	205—206 (16)	78—80	—	—	—	—	—	—	—	—

• The refraction for the grouping = N—NH— was taken equal to 5.78 [9].

•• Found %: C 69.25, 69.43; H 7.38, 7.38. $C_{11}H_{14}ON_2$. Calculated %: C 69.44; H 7.41.

was added to 0.5 mole of adduct (I), after which the reaction mixture was heated under reflux for 6 hr on the water bath. The obtained precipitate of potassium carbonate was suction filtered and washed on the filter with alcohol. The alcohol was distilled from the filtrate, and the residue was neutralized with hydrochloric acid and then extracted with benzene. After distilling off the benzene, the residue was vacum distilled to yield the desired aryltetrahydropyridazines (their constants are given in Table 2); since the latter are easily oxidized in the air and analyze poorly, they were characterized either by preparing their addition products with phenyl isothiocyanate (both the melting points of the obtained phenylthioureas after recrystallization from alcohol, and the analysis data are given in Table 2), or by obtaining the partial hydrolysis products of the starting dicarbethoxypyridazines (III, see below).

The 3-aryl-2-carbethoxy-1,2,3,6-tetrahydropyridazines (III) were obtained in the same manner as the products of the complete hydrolysis of the adducts, namely the aryltetrahydropyridazines (II), with the only difference that the amount of alkali used was cut in half.

3-o-Tolyl-2-carbethoxy-1,2,3,6-tetrahydropyridazine, m.p. 50—50.5°

Found %: C 68.21, 68.21; H 7.26, 7.38. $C_{14}H_{18}O_2N_2$. Calculated %: C 68.26; H 7.37.

Anilide of 3-o-tolyl-2-carbethoxy-1,2,3,6-tetrahydro-1-pyridazine thiocarboxylic acid (substituted phenyl-thiourea—the addition product of 3-o-tolyl-2-carbethoxy-1,2,3,6-tetrahydropyridazine to phenyl isothiocyanate), m.p. 149° (from petroleum ether).

Found %: N 10.80, 10.86. $C_{21}H_{23}O_2N_3S$. Calculated %: N 11.02.

3-p-Tolyl-2-carbethoxy-1,2,3,6-tetrahydropyridazine was characterized by obtaining the addition product with phenyl isothiocyanate (anilide of 3-p-tolyl-2-carbethoxy-1,2,3,6-tetrahydro-1-pyridazine thiocarboxylic acid), m.p. 161° (from petroleum ether).

Found %: C 66.64, 66.52; H 6.35, 6.34. $C_{21}H_{23}O_2N_3S$. Calculated %: C 66.12; H 6.08.

Arylcyclobutanes (V). The catalytic decomposition of the 3-aryl-1,4,5,6-tetrahydropyridazines was effected by heating 0.1 mole of the tetrahydropyridazine with 0.2—0.3 mole of KOH and 0.05 g of platinum catalyst (platinum oxide on clay) in a Wurtz flask. Vigorous reaction began at about 200—240°, with the evolution of gases and a partial distillation of the reaction products. In order to complete the reaction and distill off all of the

TABLE 3

Arylcyclobutanes

Aryl	Yield (in %)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated*	EM_D	Found % C	Found % H	Calculated % C	Calculated % H
o-Tolyl . .	33.5	76.5—77.0° (2.5)	1.5309	0.9398	48.13	47.68	0.45	90.21, 90.26	9.81, 9.89	90.35	9.65
m-Tolyl .	20.5	75.8—76.3 (9.5)	1.5246	0.9316	48.07	47.68	0.39	90.23, 90.24	9.78, 9.58	90.35	9.65
p-Tolyl . .	32	93.5—93.7 (11)	1.5230	0.9275	48.16	47.68	0.48	90.29, 90.42	9.71, 9.71	90.35	9.65
o-Anisyl .	14.2	84.7—84.9 (4)	1.5360	1.0098	50.10	49.32	0.78	81.40, 81.56	9.02, 8.97	81.43	8.69
p-Anisyl .	13	90.5—91 (4)	1.5320	1.0040	50.05	49.32	0.73	81.15, 81.41	8.80, 8.67	81.43	8.69

* The molecular refraction increment for the four-membered ring was taken equal to 0.48.

TABLE 4

Molar Ratios (K) of Amounts of Arylcyclobutane and Arylethylene

Aryl	Yield (in %) arylcyclobutane	Yield (in %) arylethylene	Composition of gas (in volume %) nitrogen	Composition of gas (in volume %) ethylene	K based on yields of reaction	K based on composition of the gas*
o-Tolyl . .	33.5	22	72	28	1.5	1.6
m-Tolyl . .	20.5	40	60	40	0.5	0.5
p-Tolyl .	32	28	68	32	1.1	1.1
o-Anisyl .	14.2	18.2	65	35	0.8	0.9
p-Anisyl .	13	13	68	32	1.0	1.1

* To determine K from the composition of the gas we used the equation: $K = \dfrac{a - b}{b}$,

where a is the total volume of nitrogen, b is the volume of the evolved ethylene, and a − b is the volume of nitrogen corresponding to the formation of the arylcyclobutane.

decomposition products, the temperature of the reaction mixture was raised to 300−350°. The distillate was washed with hydrochloric acid (1:1), then with 2N sodium carbonate solution, next with water, dried over calcium chloride, and finally it was vacuum distilled. The distillate (30−40 g, from several experiments) was refluxed for 30 min with sodium metal, and then redistilled in vacuo. The reaction products were isolated in the pure state by distillation through a column with a rating of 30 theoretical plates. The constants of the obtained aryl-cyclobutanes are given in Table 3.

The secondary reaction products, namely the corresponding styrenes, had the following constants: o-methyl-styrene, b.p. 43.5−44.1° (2.5 mm), and n_D^{20} 1.5441; m-methylstyrene, b.p. 45−45.5° (2.5 mm), and n_D^{20} 1.5435; p-methylstyrene, b.p. 74.5° (29 mm), and n_D^{20} 1.5397; o-methoxystyrene, b.p. 59−60.5° (4 mm),

TABLE 5

Raman Spectra of Arylcyclobutanes

o-Tolylcyclo-butane	p-Tolylcyclo-butane	m-Tolylcyclo-butane	o-Anisylcyclo-butane	p-Anisylcyclo-butane
—	218(1; φ)	221(15; ш)	224(0.5)	—
240(1)	257(2; ш)	—	265(0.5)	257(0.5; ш)
274(0.5)	—	—	—	295(0.5)
307(4)	322(4; ш)	303(5)	—	307(1)
333(2)	—	342(2)	333(5)	333(1; ш)
—	—	—	353(5)	347(1)
397(0.5)	370(2; ш)	397(1; ш)	—	—
434(1)	420(0)	439(0)	440(1.5)	410(1; ш)
460(0.5)	—	460(0)	—	460(0.5; ш)
494(0.5)	—	—	494(2)	—
530(1)	—	528(14)	530(2)	547(0.5; ш)
547(8)	547(1)	—	—	—
570(2)	590(2; ш)	584(1)	580(4)	585(0)
620(2)	621(0)	621(0)	605(0)	603(1.5)
651(3)	645(12)	651(4)	640(4)	635(12)
—	—	—	667(0.5)	671(0)
695(0)	—	695(1)	—	695(0.5)
718(4)	718(1; φ)	724(14)	724(12)	—
735(4)	738(1.5)	—	746(4)	735(1.5 ш/φ)
774(4)	792(35)	776(1)	792(10)	792(45)
802(8)	809(1)	816(7)	808(1)	827(0)
833(2)	—	—	845(2)	845(0)
862(1)	875(4)	884(0.5; ш)	877(2)	875(4)
912(1)	908(6)	912(3)	912(10)	912(8; дв/φ)
920(2)	—	—	—	—
948(1.5)	949(1.5)	947(3)	950(3)	950(1.5)
1000(4)	996(10)	1000(50)	996(15)	996(6)
1015(1)	1022(0)	1019(1.5)	1038(2)	1015(1)
1056(45)	—	—	1056(40)	1043(1)
1091(1.5)	1085(1.5)	1085(2.5)	1090(2)	1090(1)
1121(1.5)	1122(1)	1107(3)	1117(1.5)	1117(2)
1165(15)	1151(1.5)	1170(3; ш)	1167(10)	1180(25)
—	1183(10)	—	—	—
—	1198(12; φ)	—	1196(12)	—
—	1204(25)	—	1204(0)	1200(4)
1227(40)	1219(0)	1230(2)	—	1219(4)
—	1245(1.5)	1250(5)	1240(15; ш)	1248 (5; ш)
1270(6)	1270(2.5)	1270(5)	—	—
1296(8)	1305(2)	—	1304(15; ш)	1304(10; ш)
1321(1.5)	1334(2; φ)	—	—	1340(2.5)
1347(2)	1350(1.5; φ)	1342(5; ш)	1350(1)	1354(2)
1382(10)	1368(8)	1382(6)	1382(0.5)	1380(0)
1443(10)	1443(10)	1443(10)	1443(10)	1443(10)
—	1465(1)	1467(1)	—	1460(2; ш)
1493(2)	—	—	1493(8)	—
1573(2)	—	1593(5)	—	1582(2)
1606(50)	1610(30)	1610(20)	1600(50)	1612(60)

Key: ш = broad, дв; = double, ф = background.

n_D^{20} 1.5570, and d_4^{20} 1.0046; p-methoxystyrene, b.p. 62—63° (4 mm), n_D^{20} 1.5612, and d_4^{20} 1.0002.

The literature data are, respectively: b.p. 51° (9 mm), n_D^{20} 1.5447 [10]; b.p. 52—53° (9 mm), n_D^{20} 1.54 [11]; b.p. 51° (10 mm), n_D^{20} 1.5395 [11]; b.p. 83—84° (12 mm), n_D^{20} 1.5558, d_4^{20} 1.0020 [10]; b.p. 204—205° (756 mm), n_D^{18} 1.5642, d_4^{18} 1.0001 [12].

The molar ratios (K) of the amounts of arylcyclobutane and arylethylene, formed in the decomposition of the aryltetrahydropyridazines, were determined both from the yields of reaction products and the analysis of the evolved gas. • The obtained results are given in Table 4.

An ISP-51 spectrophotometer was used to take the Raman spectra of all of the synthesized arylcyclobutanes. The intensity of the lines in the spectra was estimated visually using an arbitrary scale, where the intensity of the 1443 cm^{-1} line was taken as 10 arbitrary units (Table 5). The spectra of the tolylcyclobutanes and the correspond-

---

•The ethylene contained in the gases was identified as the dibromide, b.p. 130—131°, n_D^{20} 1.5370; literature data [13]: b.p. 129—132°, n_D^{20} 1.5397.

ing anisylcyclobutanes are quite similar. * In their spectra the most intense lines are those characteristic for the disubstituted benzene ring: 640—650, 792—816, 996—1000, 1200—1240, 1600—1612 cm^{-1} [15]. The spectra also show lines in the regions 908—925 and 945—960 cm^{-1}, characteristic for the monosubstituted cyclobutane ring [16], which confirms the structure of the synthesized hydrocarbons.

SUMMARY

1. The method developed earlier for the synthesis of arylcyclobutanes, namely, the catalytic decomposition of aryltetrahydropyridazines, was used to synthesize the new o-, m- and p-tolylcyclobutanes, and the o- and p-anisylcyclobutanes.

2. The obtained arylcyclobutanes were characterized by their Raman spectra and their ultraviolet absorption spectra.

3. It was established that the hydrolysis and subsequent decarboxylation of the dicarbethoxyaryltetrahydropyridazines, the starting substances for the preparation of aryltetrahydropyridazines, go in two stages, in which connection the first to react is the carbethoxyl group found furthest away from the aryl substituent.

4. The adducts of the diethyl ester of azodicarboxylic acid with o-, m- and p-tolyl-1,3-butadienes, and with o- and p-anisyl-1,3-butadienes, were described for the first time. *

LITERATURE CITED

[1] R. Ya. Levina, M. G. Kuz'min, and Yu. S. Shabarov, Bull. Moscow State Univ., Chemistry, No. 1, 170 (1957).

[2] R. Ya. Levina, Yu. S. Shabarov, M. G. Kuz'min, N. I. Vasil'ev and E. G. Treshchova, Proc. Acad. Sci. USSR 121, 303 (1958). *

[3] A. P. Terent'ev and A. V. Dombrovskii, J. Gen. Chem 27, 2000 (1957). **

[4] K. Alder and H. Niklas, Ann. 585, 81 (1954).

[5] R. Ya. Levina, Yu. S. Shabarov, and V. K. Potapov, Bull. Moscow State Univ., Chemistry, No. 5, 201 (1958).

[6] Organic Syntheses [Russian translation] (IL, 1953), Coll: Vol. 4, p. 331.

[7] Grummitt, J. Splitter, J. Am. Chem. Soc. 74, 3924 (1952).

[8] V. R. Skvarchenko, M. G. Kuz'min, and R. Ya. Levina, Bull. Moscow State Univ., Chemistry, No. 3, 169 (1957).

[9] A. N. Kost and I. I. Grandberg, J. Gen. Chem. 26, 1717 (1956). **

[10] K. von Auwers, Lieb. Ann. 413, 295 (1917).

[11] P. P. Shorygin and N. V. Shorygina, J. Gen. Chem. 5, 555 (1935).

[12] A. Klages, A. Eppelsheim, Ber. 36, 3594 (1903).

[13] E. Erlenmeyer and H. Bunte, Ann. 168, 64 (1873).

[14] Landolt-Börnstein, Atom. u. Molekularphysik, 2 Teil, Molekeln I, (Berlin, 1951).

[15] G. S. Landsberg, P. A. Bazhulin, and M. M. Sushchinskii, Basic Parameters of Raman Spectra of Hydrocarbons [in Russian] (Izd. AN SSSR, 1956) p. 204.

[16] V. T. Aleksanyan and Kh. E. Sterin, Data of Tenth All-Union Conference on Spectroscopy [in Russian] (L'vov State Univ. Press, L'vov, 1957), Vol. 1.

---

* It should be mentioned that the Raman spectra of the xylenes and the corresponding methoxytoluenes are also very close [14].

** Original Russian pagination. See C. B. Translation.

THE SYNTHESIS OF HYDROCARBONS

LXXII. C_{10}-C_{12} DI-TERT-ALKYLMETHANES (TETRA-, PENTA-, AND HEXAMETHYLHEXANES)

R. Ya. Levina and V. K. Daukshas

Moscow State University

In previous communications [1, 2] we described a new method for the synthesis of alkanes containing two quaternary carbon atoms separated by a methylene group, the so-called di-tert-alkylmethanes (IV). The starting substance for the synthesis of these hydrocarbons was 2,4-dimethyl-1,3-pentadiene, the monohydrochloride (I) of which when reacted with organomagnesium compounds R'MgBr (first Grignard—Wurtz reaction) gave alkenes with one quaternary carbon atom (II); the hydrochlorides (III) of the latter were then subjected to a second Grignard—Wurtz reaction with alkylmagnesium halides RMgBr (in the presence of mercuric chloride), which led to the formation of di-tert-alkylmethanes (IV).

In this paper, using methylmagnesium bromide (R' = CH_3) in the first Grignard-Wurtz reaction, and ethyl- and isopropylmagnesium bromide, and also tert-butylmagnesium chloride (R = C_2H_5, iso-C_3H_7 and tert-C_4H_9), in the second Grignard—Wurtz reaction, we synthesized three new C_{10}—C_{12} di-tert-alkylmethanes with a highly branched structure (with two and three quaternary carbon atoms), and specifically, the tetra-, penta- and hexamethylhexanes.

$R = C_2H_5$, iso -C_3H_7, tert -C_4H_9.
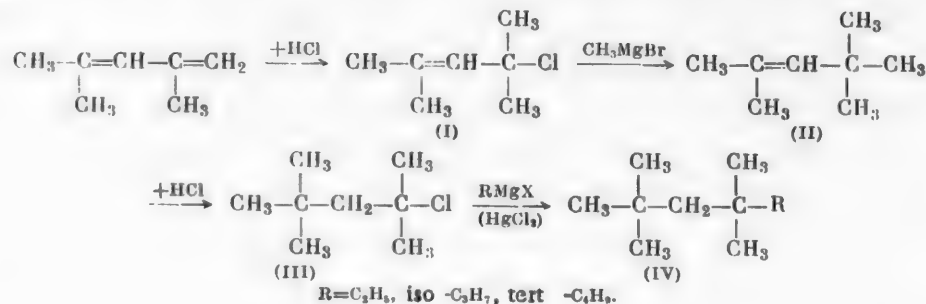
It should be mentioned that the reaction of alkylmagnesium halides (RMgX) with saturated tertiary chlorides, proceeding in the presence of mercuric chloride, leads to the formation of alkanes in small yields, from 22 to 3%, in which connection the yield drops in going from the primary alkylmagnesium halide to the secondary, and especially, to the tert-alkylmagnesium halide.

EXPERIMENTAL

Using the above scheme, and operating through the sequence of synthesizing the starting alkadiene—2,4-dimethyl-1,3-pentadiene (b.p. 92—93° at 750 mm, n_D^{20} 1.4443, d_4^{20} 0.7369; literature data [3]: b.p. 93—94° at 755 mm, n_D^{20} 1.4448, d_4^{20} 0.7375), its hydrochloride (I), and the alkene with one quaternary carbon atom—2,2,4-trimethyl-3-pentene (II; b.p. 102.5—104° at 745 mm, n_D^{20} 1.4128, d_4^{20} 0.7184; literature data [4]: b.p.

Di-tert-alkylmethanes of Structure

$$CH_3{-}\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}{-}CH_2{-}\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}{-}R$$

R	Name	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	calculated	calculated*	Found % C	H	Empirical formula	Calculated C	H	Yield in g from two expt.	in %
C_2H_5	2,2,4-Tetra-methylhexane	148.8–149.1°(745)	1.4203	0.7449	48.37	48.38	48.32	84.50, 84.33	15.70, 15.64	$C_{10}H_{22}$	84.40	15.60	31.6	22
iso-C_3H_7	2,2,4,5-Penta-methylhexane	170–170.5(757)	1.4297	0.7651	52.73	53.00	52.75	84.72, 84.94	15.30, 15.32	$C_{11}H_{24}$	84.52	15.48	23.4	15
tert-C_4H_9	2,2,3,5,5-Hexa-methylhexane	187–188(735)	1.4389	0.7830	57.18	57.62	57.20	84.54, 84.50	15.48, 15.50	$C_{12}H_{26}$	84.61	15.39	5	3

* Based on the scheme of V. M. Tatevskii [6].

103–104° at 750 mm, n_D^{20} 1.4130, d_4^{20} 0.7191; yield 60%, based on 2,4-dimethyl-1,3-pentadiene), we obtained the earlier described [1, 2] saturated tertiary chloride (III) —4-chloro-2,2,4-trimethylpentane (90% yield): b.p. 41–42° at 13 mm, n_D^{20} 1.4311, d_4^{20} 0.8748; literature data [5]: b.p. 53° at 29 mm, n_D^{20} 1.4310.

Synthesis of di-tert-alkylmethanes (IV). To react 4-chloro-2,2,4-trimethylpentane (0.5 mole) with alkyl-magnesium halides (ethyl- and isopropylmagnesium bromi-des and tert-butylmagnesium chloride, each obtained from 1.1 mole of the corresponding halide), and also to remove impurities of organomercury compounds from the reaction products, we used the method that we had developed [1, 2] to synthesize other hydrocarbons of a similar structure. The obtained di-tert-alkylmethanes (IV) were distilled through a column (35 theoretical plates), and then chromatograph-ed on silica gel. The constants, yields, and analysis data for the obtained compounds are given in the table.

A study of the Raman spectra confirmed the presence of quaternary carbon atoms in the molecules of the synthe-sized alkanes—the spectra showed intense frequencies in the regions 670–740, 930 and 1200–1250 cm^{-1} [7].

SUMMARY

Using the method developed earlier, we synthesized some new C_{10}–C_{12} di-tert-alkylmethanes with two and three quaternary carbon atoms, and specifically, we syn-thesized 2,2,4,4-tetramethyl-,2,2,4,4,5-pentamethyl-,and 2,2,3,3,5,5-hexamethylhexane.

LITERATURE CITED

[1] R. Ya. Levina, Yu. S. Shabarov, V. K. Daukshas, and E. G. Treshchova, Proc. Acad. Sci. USSR 113, 1286 (1957).*

[2] R. Ya. Levina, Yu. S. Shabarov, and V. K. Dauk-shas, J. Gen. Chem. 28, 2049 (1958).*

[3] R. Ya. Levina, A. A. Fainzil'berg, and N. P. Shu-sherina, J. Gen. Chem. 18, 1775 (1948).

[4] R. Ya. Levina and Yu. B. Kagan, J. Gen. Chem. 11, 523 (1941).

[5] F. C. Whitmore and H. A. Southgate, J. Am. Chem. Soc. 60, 2571 (1938).

[6] V. M. Tatevskii, The Chemical Structure of Hy-drocarbons and Regularities in Their Physicochemical Pro-perties [in Russian] (Izd. MGU, 1953) pp. 287–296.

[7] B. I. Stepanov, J. Phys. Chem. [USSR] 20, 917 (1946).

Received November 24, 1958

* Original Russian pagination. See C. B. Translation.

AROMATIC HYDROCARBONS

XI. REACTION OF PHOSPHORUS PENTOXIDE WITH PHENYLTETRAHYDROPHTHALIC ACIDS AND THEIR ANHYDRIDES (ADDUCTS OF "DIENE SYNTHESIS")

V. R. Skvarchenko, R. Ya. Levina and M. I. Pugina

Moscow State University

As we had shown earlier [1], alkyltetrahydrophthalic anhydrides—the products of the "diene synthesis" of 1,3-alkadienes with either maleic or alkylmaleic anhydrides—when heated with phosphorus pentoxide cleave two molecules of carbon monoxide and a molecule of water, and are converted to aromatic hydrocarbons of the benzene series.
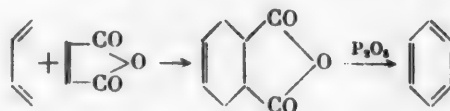
However, if a phenyl group is found in the 1 position of the dienic hydrocarbon, then the adduct with maleic anhydride, being 3-phenyl-1,2,3,6-tetrahydrophthalic anhydride, reacts in a different manner with phosphorus pentoxide, without the cleavage of carbon monoxide, and leading to the formation of fluorene [2].
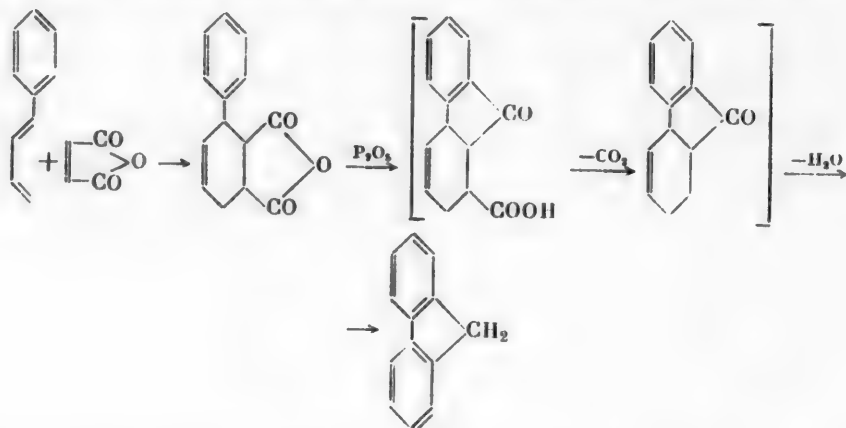
As can be seen from the given equation, the formation of fluorene• goes through the stage of the intramolecular acylation of the benzene ring by the anhydride group.

• This reaction, simplified in the respect that the adducts of various alkadienes with cinnamic acid (2-phenyltetrahydrobenzoic acids) were reacted with phosphorus pentoxide, was worked out as a method for the synthesis of hydrocarbons of the fluorene series [2].

As a result, tetrahydrophthalic acids and their anhydrides—adducts of the "diene synthesis"—when reacted with phosphorus pentoxide, can, depending on their structure, be converted to aromatic hydrocarbons via two reactions that differ in principle: 1) Alkyltetrahydrophthalic anhydrides, when reacted with phosphorus pentoxide, suffer the first type of aromatization reaction—a simultaneous decarbonylation and dehydration with the formation of hydrocarbons of the benzene series; and 2) 3-Phenyl-1,2,3,6-tetrahydrophthalic anhydride, when reacted with the same reagent, suffers the second type of aromatization reaction—in this case carbon monoxide is not cleaved, and the final reaction products prove to be fluorene or its homologs.

In this paper we studied the reaction of phosphorus pentoxide with those phenyltetrahydrophthalic acids (or their anhydrides) having the phenyl substituent in other than the 3-position with respect to the carboxyl group. Thus, we heated 2-phenyl-1,2,3,6-tetrahydrophthalic acid (I) (from the adduct of butadiene with phenylmaleic anhydride) with phosphorus pentoxide; the reaction product in this case proved to be fluorene (50% yield). The same was true for 3-phenyl-1,2,3,6-tetrahydrophthalic anhydride; when 2-phenyl-1,2,3,6-tetrahydrophthalic acid was reacted with phosphorus pentoxide it suffered aromatization via the second type—the reaction went through the stage of acylation of the phenyl ring by the carboxyl group and subsequent conversion of the intermediate hydroaromatic ketone to fluorene.
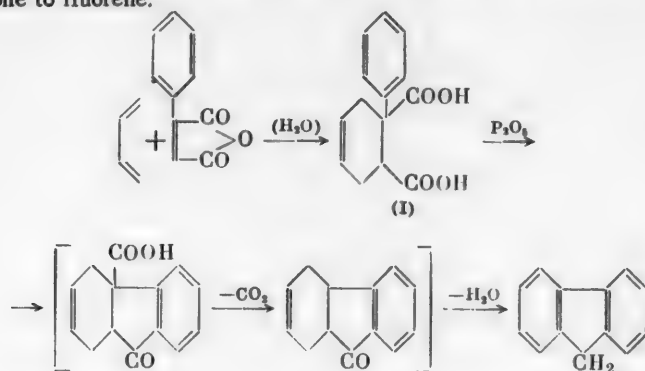
It should be mentioned that 2-phenyl-1,2,3,6-tetrahydrophthalic acid proved to be more stable than the anhydride of the isomeric 3-phenyl-1,2,3,6-tetrahydrophthalic acid when heated with phosphorus pentoxide, and here, besides fluorene, the original acid was isolated from the reaction products.

We also reacted phosphorus pentoxide with 4-phenyl-1,2,3,6-tetrahydrophthalic anhydride (II) (adduct of 2-phenyl-1,3-butadiene with maleic anhydride), where the phenyl substituent was at some distance from the anhydride grouping, which excluded the possibility of intramolecular acylation, and here only biphenyl was isolated as the sole reaction product (65% yield).
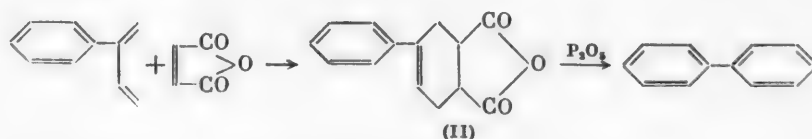
As a result, if the starting phenyltetrahydrophthalic anhydride has the phenyl ring at some distance from the anhydride grouping and acylation cannot take place, then when the adduct is reacted with phosphorus pentoxide the aromatization goes via the first type , with simultaneous decarbonylation and dehydration.

4,5-Diphenyl-1,2,3,6-tetrahydrophthalic anhydride (III) (adduct of 2,3-diphenyl-1,3-butadiene with maleic anhydride) proved to be stable when heated with phosphorus pentoxide.
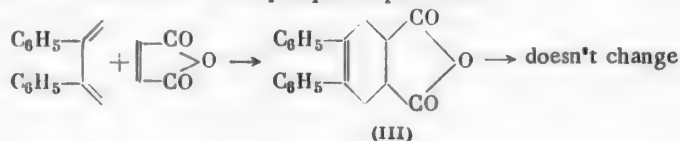
EXPERIMENTAL

2-Phenyl-1,2,3,6-tetrahydrophthalic acid (I) was obtained by heating a mixture of butadiene (7.1 ml, 0.1 mole) and phenylmaleic anhydride • (8.7 g, 0.05 mole, m.p. 118°) in benzene (10 ml), in the presence of a small amount of hydroquinone, in an autoclave at 50° for 24 hr. The reaction product was extracted with 5% sodium bicarbonate solution; acidification of the solution gave 10 g (80%) of acid (I) with m.p. 196° (literature data [4]: m.p. 196—197°).

4-Phenyl-1,2,3,6-tetrahydrophthalic anhydride (II) was obtained by heating equimolar amounts of 2-phenyl-1,3-butadiene • • and maleic anhydride (22.4 g, 0.23 mole) in benzene solution (112 ml) on the boiling water bath for 4 hr. Anhydride (II) (9.3 g, 16% yield, based on starting phenylacetoxybutene) had m.p. 105° (literature data [5]: m.p. 105°).

4,5-Diphenyl-1,2,3,6-tetrahydrophthalic anhydride (III) was obtained by heating a mixture of 2,3-diphenyl-1,3-butadiene • • (5.35 g, 0.026 mole) and maleic anhydride (2.55 g, 0.026 mole) in benzene under reflux for 2 hr. We obtained 7.5 g of (III) (20% yield, based on starting acetophenone pinacol • •), m.p. 161—163° (literature data [6]: m.p. 164.5°).

Reaction of phenyltetrahydrophthalic acid and phenyltetrahydrophthalic anhydrides with phosphorus pentoxide. A mixture of 2-phenyl-1,2,3,6-tetrahydrophthalic acid (I) (8 g, 0.036 mole) and phosphorus pentoxide (4.5 g, 0.036 mole) was heated gradually in a Wurtz flask; the reaction was accompanied by tarring and the brisk evolution of carbon dioxide. The reaction product was removed immediately by distillation, heated with concentrated caustic solution (to remove unreacted adduct), and recrystallized twice from alcohol. The isolated fluorene (3 g, 50% yield) had m.p. 113°; picrate m.p. 78—79°, which agrees with the literature data [7]. The mixed melting points with authentic fluorene and with the picrate were not depressed.

A mixture of 4-phenyl-1,2,3,6-tetrahydrophthalic anhydride (II) (9.3 g, 0.04 mole) and phosphorus pentoxide (5.7 g, 0.04 mole) was heated gradually in a Wurtz flask until the evolution of carbon monoxide ceased; the reaction product was distilled off, heated with 2N caustic solution (to remove possible unreacted anhydride), and recrystallized from alcohol. The obtained biphenyl (4.2 g, 66% yield) melted at 69—70°, which agrees with the literature data [8], and did not depress the melting point when mixed with authentic biphenyl.

From 4,5-diphenyl-1,2,3,6-tetrahydrophthalic anhydride (III) (0.043 mole), by heating under similar conditions with phosphorus pentoxide (4.5 g, 0.043 mole), we isolated by distillation a substance (8.8 g, 67.7% yield) that, after recrystallization from methyl alcohol, melted at 161°, and did not depress the melting point when mixed with the starting anhydride.

SUMMARY

1. It was shown that when phosphorus pentoxide is reacted with phenyltetrahydrophthalic acids (or their anhydrides), having the phenyl substituent in different positions with respect to the carboxyl group, the latter are converted to aromatic hydrocarbons via two reactions, which differ in their character.

2. The reaction of phosphorus pentoxide with 2-phenyl-1,2,3,6-tetrahydrophthalic acid (from the adduct of butadiene with phenylmaleic anhydride) results in acylation of the phenyl ring by the carboxyl group and the cleavage of carbon dioxide with subsequent transformation of the intermediate hydroaromatic ketone to fluorene (50% yield).

4-Phenyl-1,2,3,6-tetrahydrophthalic anhydride (adduct of 2-phenyl-1,3-butadiene with maleic anhydride), when reacted with phosphorus pentoxide, suffers simultaneous cleavage of carbon monoxide and dehydration, and is converted to biphenyl (65% yield).

• The compound was obtained by the Reformatskii reaction, by reacting ethyl bromoacetate with ethyl benzoylformate, followed by the cleavage of water from the obtained phenylhydroxysuccinic acid [3].
• • 2-Phenyl-1,3-butadiene (obtained by the pyrolysis of 2-phenyl-4-acetoxy-1-butene at 650° [5] and 2,3-diphenyl-1,3-butadiene (obtained by the dehydration of the acetophenone pinacol with potassium bisulfate [6] were not isolated in the pure state, since they polymerize with extreme ease, and instead were reacted immediately with maleic anhydride.

LITERATURE CITED

[1] R. Ya. Levina, V. R. Skvarchenko, V. N. Kostin, and N. S. Kataeva, Proc. Acad. Sci. USSR 91, 95 (1953). R. Ya. Levina, V. R. Skvarchenko, N. S. Kataeva, and E. G. Treshchova, J. Gen. Chem. 23, 1998 (1953)*; V. R. Skvarchenko, R. Ya. Levina, and T. V. Kostroma, J. Gen. Chem. 25, 1094 (1955)*; V. R. Skvarchenko, R. Ya. Levina, and M. G. Kuz'min, J. Gen. Chem. 27, 1784 (1957).*

[2] R. Ya. Levina, V. R. Skvarchenko, L. A. Chervoneva, L. V. Fedorchuk, and T. T. Vasil'eva, Proc. Acad. Sci. USSR 118, 938 (1958).*

[3] C. S. Rondestvedt Jr. and A. Filbey, J. Org. Chem. 19, 119 (1954).

[4] L. Miller, D. Mann, J. Am. Chem. Soc. 72, 1484 (1950).

[5] C. Price, F. Benton, C. Schmidle, J. Am. Chem. Soc. 71, 2860 (1949).

[6] K. Alder, J. Haydn, Lieb. Ann. 570, 212 (1950).

[7] N. Zelinsky, L. Titz and M. Gaverdowskaja, Ber. 59, 2591 (1926); P. Barbier, Ann. chim. (5) 7, 479 (1876).

[8] W. Zartman and H. Adkins, J. Am. Chem. Soc. 54, 3398 (1932).

---

* Original Russian pagination. See C. B. Translation.

STEREOCHEMISTRY OF NITROGEN HETEROCYCLES

V. STEREOISOMERISM OF 2-METHYL-4-HYDROXYDECAHYDROQUINOLINE

D. V. Sokolov, G. S. Litvinenko, and K. I. Khludneva

Institute of Chemical Sciences, Academy of Sciences of the Kazakh SSR

A study of the stereoisomerism of 2-methyl-4-ketodecahydroquinoline and the working out of methods for the synthesis of all of the four theoretically possible racemic ketones (Scheme 1)[1], made it possible to under-take a systematic study of the conditions for the reduction of these compounds, and thus go from the series of stereoisomeric ketones to the voluminous series of stereoisomeric alcohols of 2-methyl-4-hydroxydecahydroquino-line, possessing great interest in medicinal chemistry.

Scheme 1

(I) α-Isomer,
(Ia) N-Benzoyl-,

(II) β-Isomer
(IIa) N-Benzoyl-,

(III) Hydrochloride,
m. p. 199°

(IV) γ-Isomer, 42°
(IVa) N-Benzoyl-,

(V) δ-Isomer,
(Va) N-Benzoyl-,

(VI) Hydrochloride
m. p. 210°

(VII) Hydrate of the
γ-isomer
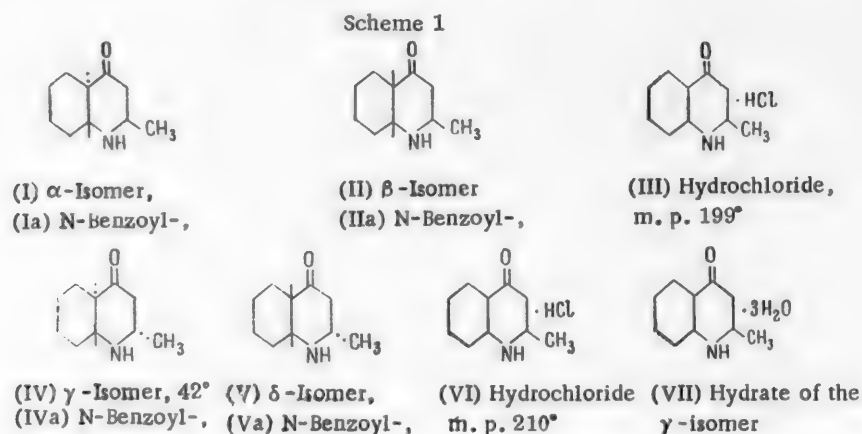
In a previous paper [2] we had described techniques for the reduction and catalytic hydrogenation of the α- and β-stereoisomers of 2-methyl-4-ketodecahydroquinoline (I) and (II), their hydrochloride (III), and the N-ben-zoyl derivatives (Ia) and (IIa). We depicted the spatial structure of the four alcohols obtained in this manner, and the starting α- and β-ketones, by the conformations shown in Scheme 2.

As a result, the hydrogenation and reduction of the α- and β-ketone bases (Ib) and (IIb), showing mutual isomerization in these processes, and the catalytic hydrogenation of their stable benzoyl derivatives (Ia) and (IIa), permitted obtaining all four racemic alcohols (VIII), (IX), (X) and (XI), and established their structural similarity to the corresponding α- and β-ketones. Due to the overloading of the molecule with axial substituents, it is possible for alcohol (XI) to have an inverted conformation, with the hydroxyl group in the equatorial position [2].

In this paper we describe the reduction of a second pair of stereoisomers of 2-methyl-4-ketodecahydroquino-line, and specifically, the reduction of γ-ketone (IV), the N-benzoyl derivatives (IVa) and (Va) of the γ- and δ-ketones, the hydrochloride (VI), and the hydrate (VII).

The conformations and steric relationships of the second pair of γ- and δ-ketones and of hydrochloride (VIa) are shown in Scheme 3. In this scheme the δ-ketone is shown as its N-benzoyl derivative with m.p. 118°, easily

Scheme 2

(Ib) α-Isomer,   (IIb) β-Isomer

(VIII)   (IX)   (X)   (XI)

Trans-series   Cis-series
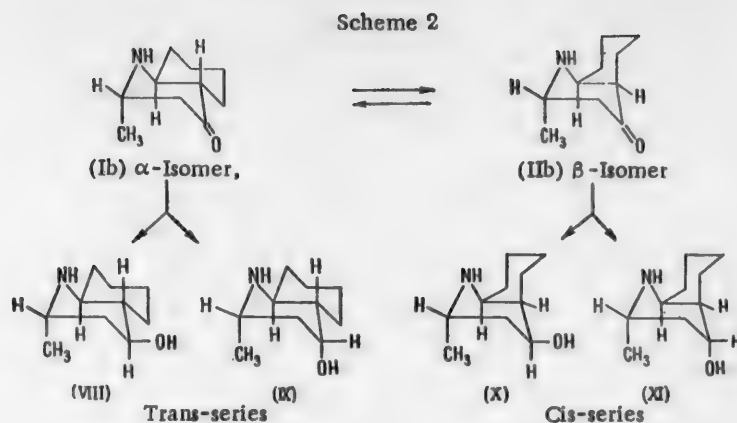
obtained by the benzoylation of hydrochloride (VIa) in aqueous solution at the moment of its decomposition with alkali. Here it must be assumed that in the benzoylation reaction, together with the cation of hydrochloride A, the conformation of the cation of hydrochloride B takes part in the form of two "bathtubs," from which benzamide (Vb) is formed, and through which, consequently, the isomerization of the γ-ketone to the δ-ketone occurs [1]. The cation of hydrochloride A, in the form of two "armchairs" forms during the benzoylation, corresponding to the position of equilibrium, the benzoyl derivative of the γ-ketone (IVb), not shown in Scheme 3.

The two pairs of stereoisomeric alcohols (XII) and (XIII), on the one hand, and (XIV) and (XV), on the other hand, corresponding respectively to the structure of the γ- and δ-ketones (IVb) and (Vb), show the same order of coupling of the piperidine and cyclohexane rings [2] as in the first two pairs of alcohols (VIII, IX) and (X, XI), obtained respectively from the α- and β-ketones (Ib) and (IIb) (Scheme 2), and differ from the latter in having the methyl radical in the equatorial position.

As the result of studying the reduction products of the γ- and δ-ketones (IVb) and (Vb), we obtained three of the four theoretically possible racemates of 2-methyl-4-hydroxydecahydroquinoline (XII—XIV), but have not succeeded as yet in obtaining racemate (XV). The melting points of the alcohols and their derivatives are given in Table 1.

Scheme 3

(VIa)   A   B

C_6H_5COCl, NaOH

(IVb) γ-Isomer   (Vb) N-Benzoyl-δ-isomer

(XII)   (XIII)   (XIV)   (XV)

Trans-series   Cis-series
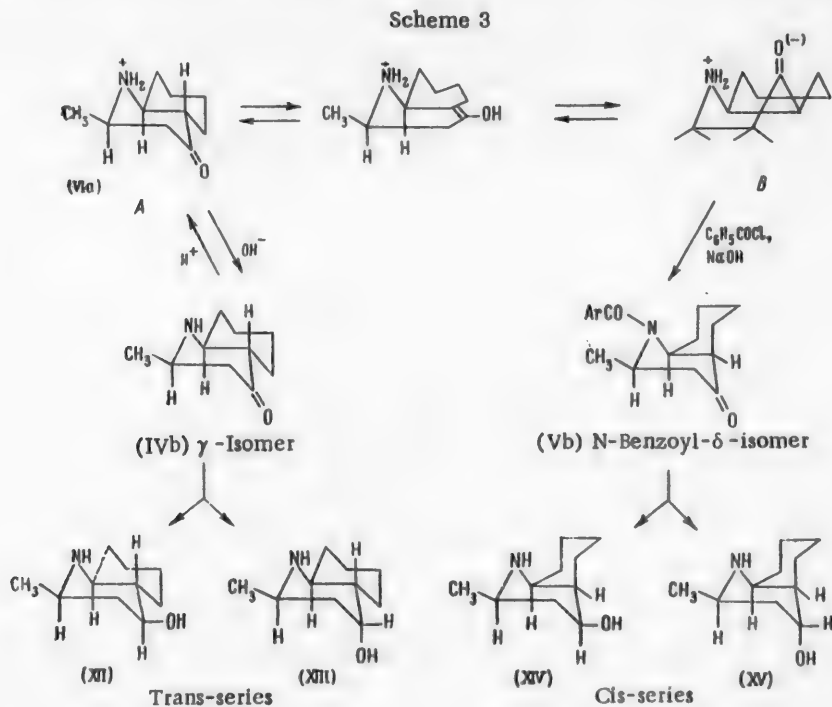
Alcohol (XII) is most easily obtained (74% yield) by the reduction of the γ-ketone (IVb) with sodium metal in alcohol solution, while its epimer (XIII), under the same reduction conditions, was isolated in a total yield of only 3%. When the same ketone (IVb) was hydrogenated using Ni catalyst, in benzine solution, the yields of the indicated alcohols (XII) and (XIII) were 44 and 36%, respectively, and when the reduction was run in alcohol solution, the yields were 64 and 23% respectively. *

The catalytic hydrogenation, using Ni catalyst, of 2-methyl-4-ketodecahydroquino line hydrochloride (VIa), obtained from the γ-ketone (IVb) and from the hydrate (VII), yields two alcohols—(XII) (39%) and (XIII) (59%). corresponding to the γ-ketone (IVb), and fails to give any alcohols with the configuration of the δ-ketone (Vb). As a result, here we have a repetition of already known facts, described [2] in the analogous hydrogenation of hydrochloride (III) with m.p. 199°, formed by the α- and β-ketones (I) and (II) (Scheme 1). Evidently, the conformation of cation A of hydrochloride (VIa), in the form of two armchairs, is also more sterically suitable for catalytic hydrogenation in the given case than is the conformation of cation B in the form of two bathtubs. For this reason, equilibrium in the system A $\rightleftharpoons$ B, when hydrogenation is in aqueous solution, must be assumed to be shifted completely toward the first cation, as a result of which the possibility of forming alcohols (XIV) and (XV) becomes quite improbable.

As was to be expected, the catalytic hydrogenation of an aqueous suspension of hydrate (VII) gave the known alcohols (XII) and (XIII) in yields of 48 and 33%, respectively. These racemates, (XII) and (XIII), are also obtained as the sole products when the benzoyl derivative (IVa) of the γ-ketone (IVb) is hydrogenated, and for this reason their structural similarity to this ketone is without doubt. Alcohol (XII), when crystallized from aqueous solution, adds three molecules of water, and melts at 92°. As a result, the ability of γ-ketone (IVb) to form hydrate (VII), is transferred to only one of the two alcohols formed from it on reduction and hydrogenation. The stereoisomeric alcohol (XIV), corresponding to the conformation of the δ-ketone, is obtained in good yield (92%) by the catalytic hydrogenation of the N-benzoyl compound (Vb) (m.p. 118°) in the presence of nickel catalyst. Under these hydrogenation conditions, the epimeric alcohol (XV) is probably not formed at all.

Scheme 4
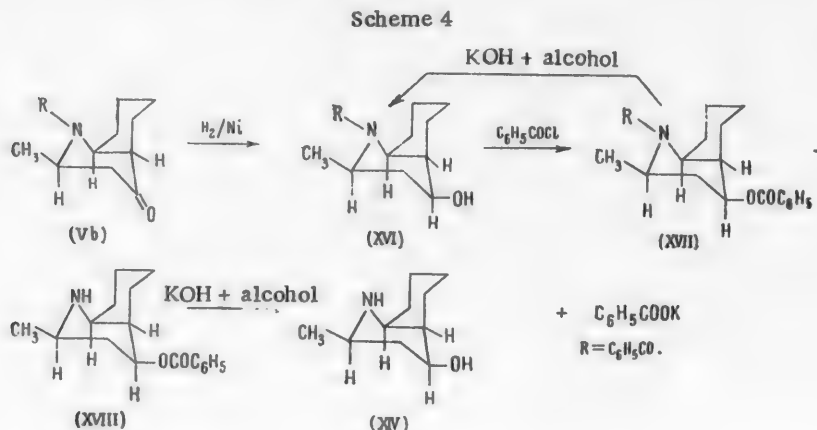
The benzoyl radical of alcohol (XVI) cannot be cleaved by refluxing with either alcoholic KOH solution or dilute hydrochloric acid. For this reason, to obtain the alcohol-base (XIV), we ran the benzoylation of (XVI) in such manner that the acyl radical was partially cleaved, due to the hydrogen chloride liberated during the benzoylation, and this led to the formation of the two benzoates (XVII) and (XVIII), in approximately equal amounts. Saponification of the dibenzoyl compound (XVII) in alcoholic KOH solution, and repeating the benzoylation of (XVI), enabled us to convert this amide completely to benzoate (XVIII), from which it is an easy matter to obtain alcohol (XIV) with m.p. 114—115° (Scheme 4).

The yields of the alcohols (XII), (XIII) and (XIV), using different techniques to reduce the γ- and δ-ketones, are summarized in Table 2.

_____

* In all cases, the amount of the alcohols needed to bring the material balance up to 100% remains as the unseparated mixture.

TABLE 1

Compound	Alcohols		
	(XII), m. p. 143-144°	(XIII), m. p. 157-158°	(XIV), m. p. 114-115°
Hycrochloride	311—312°	247—248°	278—279°
Picrate	207—208	195—196	160—161
N-Benzoyl	131—132	133—134	182—183
Hydrate	91— 92	—	—

TABLE 2

Expt. No.	Ketone and derivatives	Solvent	Yield of alcohols (in %)		
			(XII), m.p. 143-144°	(XIII), m.p. 157-158°	(XIV), m.p. 114-115°
1	γ-Ketone (IVb)	Alcohol	74.0	2.7	—
		Alcohol	64.3	22.7	—
		Benzine	43.6	35.9	—
2	Hydrochloride (VI)	Water	38.8	59.0	—
3	Hydrate (VII)	Water	42.2	32.6	—
4	N-Benzoyl (IVa)	Alcohol	8.9	61.9	—
5	N-Benzoyl (Va)	Alcohol	—	—	92.3

Note. The reduction method in Expt. 1 was Na+alcohol, and in Expt. Nos. 2-5 it was H_2 + Ni-catalyst.

Alcohol (XII), obtained in good yield when ketone (IVb) is reduced with sodium in alcohol, and in compara-tively smaller yield when catalytic hydrogenation is employed, should be stable (Auwers—Skita rule), and ac-cording to the principles of conformational analysis [3], should have the hydroxyl group in the equatorial position, while alcohol (XIII) should correspondingly have the hydroxyl group in the axial position. The solitary racemate (XIV) belonging to the cis-series, and evidently formed in the catalytic hydrogenation of the δ-ketone (Vb) due to attack of the carbonyl group by activated hydrogen predominantly from the axial region (Scheme 5, shown by arrow), apparently has the hydroxyl group in the equatorial position.

Scheme 5
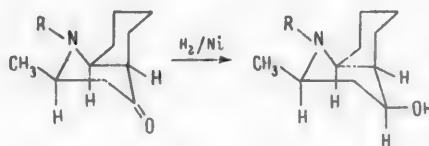
As a result, a study of the reduction and catalytic hydrogenation of the stereoisomers of 2-methyl-4-keto-decahydroquinoline and their four N-benzoyl derivatives permitted obtaining seven of the eight theoretically possi-ble racemates of 2-methyl-4-hydroxydecahydroquinoline, and it also made many of them available for the syn-thesis of new medicinals. The conformations of the above described four stereoisomeric ketones, and of the seven racemic alcohols corresponding to them, will be examined further when we discuss the results of the optical studies.

EXPERIMENTAL

The γ-isomer of 2-methyl-4-ketodecahydroquinoline (IVb) with m.p. 41—42°, its 1-benzoyl derivative (IVa) with m.p. 138—139°, and the 1-benzoyl derivative of the δ-isomer (Vb) with m.p. 117—118°, used in the

present study, were obtained as described earlier [1]. The Raney nickel catalyst was prepared as follows [4]: 10 g of Ni-Al alloy was added in 2 g portions every 10 min to 100 ml of 30% sodium hydroxide solution. The catalyst was heated on the water bath for 30 min in such manner that the temperature reached 70°, after which the alkali was leached out with small portions of water (1 liter). In the cases where the hydrogenation was run in organic solvents, the catalyst was washed further with alcohol and the proper solvent.

Hydrogenation of the γ-isomer of 2-methyl-4-ketodecahydroquinoline (IVb) on Raney Ni catalyst in alcohol solution. The nickel catalyst, obtained from 10 g of nickel-aluminum alloy, and previously saturated with hydrogen, was added to a solution of 30 g of the γ-isomer (IVb), m.p. 41–42°, in 200 ml of alcohol. The hydrogenation was stopped after shaking for 1.5 hr, and here 4.4 liters of hydrogen was absorbed, as compared to theoretical of 4.6 liters. Another 140 g of the γ-isomer (IVb) was hydrogenated under similar conditions. The products were combined, the catalyst was filtered, then washed with alcohol, and the alcohol was distilled from the filtrate to dryness. The residue of bases was dissolved in anhydrous alcohol, and then neutralized to Congo with an alcohol solution of dry hydrogen chloride. The mixture of hydrochlorides was recrystallized from anhydrous alcohol. We obtained 122.4 g of the hydrochloride of 2-methyl-4-hydroxydecahydroquinoline (XII) with m.p. 311–312°.

Found %: N 6.89, 6.56, $C_{10}H_{20}ONCl$. Calculated %: N 6.81.

A solution of 20.0 g of the hydrochloride in water was treated with excess potassium carbonate solution, after which the base was extracted with chloroform, and the extract dried over fused potassium carbonate. Removal of the solvent and recrystallization of the residue from acetone gave 15.9 g of 2-methyl-4-hydroxydecahydroquinoline (XII) with m.p. 143–144°.

Found %: C 71.18, 70.94; H 11.28, 11.22; N 8.41, 8.31. $C_{10}H_{19}ON$. Calculated %: C 70.96; H 11.31; N 8.28.

When recrystallized from water, alcohol (XII) crystallizes with three molecules of water, and melts in a sealed capillary at 91–92°. In an open capillary it melts the same as the anhydrous form (143–144°).

Found %: H_2O 25.1. M 222.6. $C_{10}H_{19}ON \cdot 3H_2O$. Calculated %: H_2O 24.1. M 223.3.

The hydrochloride was obtained by neutralizing the free base (XII) with an alcoholic solution of dry hydrogen chloride; tiny tetragonal colorless plates with m.p. 311–312° (from anhydrous alcohol), not depressing the melting point when mixed with the described specimen.

The picrate was obtained as yellow crystals with m.p. 207–207.5° (from a mixture of anhydrous alcohol and petroleum ether).

Found %: N 14.43, 14.17. $C_{16}H_{22}O_8N_4$. Calculated %: N 14.06.

1-Benzoyl-2-methyl-4-hydroxydecahydroquinoline. A solution of 1.5 g of alcohol (XII) in 90 ml of dry benzene was mixed with a solution of 0.62 g of benzoyl chloride in 15 ml of benzene. The hydrochloride of isomer (XII), obtained as a precipitate when the mixture was allowed to stand overnight, was separated and washed with benzene (0.83 g of crystals with m.p. 311–312° was obtained, not showing a melting point depression when mixed with the specimen), after which the benzene solution was washed with water, dried over potassium carbonate, and evaporated to a small volume. The N-benzoyl derivative was recrystallized from a mixture of benzene and benzine. We obtained 0.87 g (73%) of the 1-benzoyl-2-methyl-4-hydroxydecahydroquinoline isomer of (XII) with m.p. 131–132°.

Found %: N 5.75, 5.66, $C_{17}H_{23}O_2N$. Calculated %: N 5.13.

The alcohol solution remaining after the removal of the hydrochloride of (XII), was evaporated to dryness, the dry residue of salts was decomposed with aqueous potassium carbonate solution, and the free base was extracted with chloroform, dried over potassium carbonate and, after removal of the solvent, was recrystallized from dioxane. We obtained 35.6 g of the isomer of 2-methyl-4-hydroxydecahydroquinoline (XIII) as tiny colorless scales with m.p. 157–158°.

Found %: C 70.42, 70.51; H 11.45, 11.40; N 8.30, 8.21. $C_{10}H_{19}ON$. Calculated %: C 70.96; H 11.31; N 8.28.

The picrate was obtained by mixing equivalent amounts of the base (XIII) and picric acid in anhydrous alcohol. Yellow rods with m.p. 195–196° (from a mixture of anhydrous alcohol and petroleum ether).

Found %: N 14.31, 14.24. $C_{16}H_{22}O_3N_4$. Calculated %: N 14.06.

The hydrochloride was obtained as clusters of tiny white needles with m.p. 247—248° (by precipitation from anhydrous alcohol with ether).

Found %: N 6.63, 6.73. $C_{10}H_{20}ONCl$. Calculated %: N 6.81.

1-Benzoyl-2-methyl-4-hydroxydecahydroquinoline was obtained by the benzoylation of isomer (XIII) in benzene solution, as described above. Fine colorless crystals with m.p. 133—134° (from acetone).

Found %: N 5.50, 5.42. $C_{17}H_{23}O_2N$. Calculated %: N 5.13.

From the remaining mixture of isomeric alcohols (XII) and (XIII), after two alternate recrystallizations of their hydrochlorides from anhydrous alcohol, and of the free bases from dioxane, we obtained an additional 12.0 g of the hydrochloride of isomer (XII) with m.p. 311-312°, and 3.5 g of isomer (XIII) with m.p. 157-158°. As a result, we obtained a total yield of 134.4 g (64.3%) of the hydrochloride of 2-methyl-4-hydroxydecahydroquinoline (XII) with m.p. 311-312° [the alcohol-base (XII) has m.p. 143-144°], and 39.1 g (22.7%) of isomeric alcohol (XIII) with m.p. 157-158°.

Hydrogenation of the γ-isomer of 2-methyl-4-ketodecahydroquinoline (IVb) on nickel catalyst in benzine solution. A solution of 19.3 g of the γ-isomer (IVb), m.p. 41—42°, in 60 ml of dry benzine (b.p. 80—100°) was hydrogenated in the presence of Raney Ni catalyst (the catalyst was prepared from 10 g of the alloy, as described above, washed with anhydrous alcohol, then with benzine, and finally it was saturated with hydrogen in 40 ml of benzine). The hydrogenation was stopped after 6 hr (amount of hydrogen abosrbed was 1.55 liters, and the hydrogenation product had begun to crystallize), and a new portion of catalyst (from 10 g of the alloy) in 50 ml of benzine was added to the hydrogenation flask. The calculated amount of hydrogen (3 liters) was absorbed after shaking for an additional 3 hr. The catalyst was filtered, washed with benzine, then with alcohol, and the combined filtrates were evaporated to dryness. After a 3-fold alternate recrystallization of the hydrogenation products, as the hydrochlorides from anhydrous alcohol, and as the free bases from dioxane, we obtained 10.36 g (43.6%) of the hydrochloride with m.p. 311—312°, corresponding to the isomer of 2-methyl-4-hydroxydecahydroquinoline (XII) with m.p. 143—144°, and 7.0 g (35.9%) of the isomeric alcohol (XIII) with m.p. 157—158°. Both compounds failed to depress the melting point when mixed with the described specimens.

Reduction of the γ-isomer of 2-methyl-4-hydroxydecahydroquinoline (IVb) with sodium metal in alcohol solution. To a solution of 11.0 g of the γ-isomer (IVb), m.p. 41—42°, in 400 ml of anhydrous alcohol, was added, in small portions, 30 g of sodium metal in 45 min. Toward the end of reaction the liquid was heated on the boiling water bath until all of the sodium had dissolved (30 min). After cooling, the deep red solution was treated in small portions with 140 ml of concd. hydrochloric acid with cooling. The deposited sodium chloride was filtered and washed with alcohol, the alcohol and part of the water were distilled off under a slight vacuum, and the aqueous residue was washed with chloroform to remove neutral tars, and then it was decomposed with excess potassium carbonate. The free base was extracted with chloroform, dried over potassium carbonate, and after distilling off the chloroform, the residue was dissolved in anhydrous alcohol and then neutralized with an alcohol solution of dry hydrogen chloride. The obtained mixture of hydrochlorides was recrystallized from anhydrous alcohol, and here we obtained 10.0 g (73.9%) of the hydrochloride with m.p. 311—312°, corresponding to the isomeric alsohol (XII) with m.p. 143—144°. The remainder of the salts was converted in the usual manner to the free bases, the recrystallization of which from dioxane gave 0.3 g (2.7%) of the isomeric alcohol (XIII) with m.p. 157—158°. The obtained hydrochloride and alcohol-base failed to depress the melting point when mixed with the proper specimens. The residue of unseparated mixture weighed 1.4 g (12.6%).

Hydrogenation of the hydrate of the γ-isomer of 2-methyl-4-ketodecahydroquinoline (VII). A suspension of 21.5 g of finely powdered hydrate (VII), m.p. 55—56°, in 250 ml of water was hydrogenated in the presence of nickel catalyst, prepared from 10 g of the nickel-aluminum alloy, and previously saturated with hydrogen in 30 ml of water. The amount of hydrogen absorbed in 4 hr was 2.4 liters, as compared to a theoretical 2.46 liters. The catalyst was filtered and washed with water, while the aqueous solution was acidified with hydrochloric acid and then evaporated to dryness under a slight vacuum (the residue weighed 18.0 g). The mixture of isomeric alcohols was separated by the alternate 4-fold recrystallization of their hydrochlorides from anhydrous alcohol, and of the free bases from dioxane. We obtained 9.72 g (48.2%) of the hydrochloride with m.p. 311—312°, corresponding to the isomer of 2-methyl-4-hydroxydecahydroquinoline (XII) with m.p. 143—144°, and 5.35 g (32.6%) of alcohol (XIII) with m.p. 157—158°.

Hydrogenation of the hydrochloride of the γ-isomer of 2-methyl-4-ketodecahydroquinoline (VIa). A solution of 27.7 g of hydrochloride (VIa), m.p. 209—210°, in 150 ml of water was hydrogenated in the presence of nickel catalyst, prepared from 10 g of the nickel-aluminum alloy, and previously saturated with hydrogen in 30 ml of water. The amount of hydrogen absorbed in 5 hr was 3.4 liters, as compared to the 3.5 liters required by theory. Another 28.0 g of hydrochloride (VIa) was hydrogenated under the same conditions. The products from the two hydrogenations were combined, the catalyst was filtered and washed with hot water, and the filtrate was evaporated to dryness, using a water-jet pump. After alternate 3-fold recrystallization of the mixture of isomeric alcohols as the hydrochlorides from anhydrous alcohol, and as the free bases from dioxane, we obtained 21.8 g (38.8%) of the hydrochloride with m.p. 311-312°, corresponding to the alcohol (XII) with m.p. 143-144°, and 27.3 g (59%) of the alcohol-base (XIII) with m.p. 157-158°, neither depressing the melting point when mixed with the proper specimen, described above. The residue weighed 0.4 g (0.9%).

Hydrogenation of the γ-isomer of 1-benzoyl-2-methyl-4-ketodecahydroquinoline (IVa). A solution of 47.4 g of the γ-isomer (IVa), m.p. 138—139°, in 230 ml of alcohol was hydrogenated in the presence of nickel catalyst, obtained from 10 g of the alloy. The amount of hydrogen abosrbed after shaking for 16 hr was 3.6 liters, and then a similar portion of the catalyst was added to the hydrogenation flask, after which the hydrogenation was ended in 1.5 hr. The calculated amount of hydrogen (4.5 liters) was absorbed. The catalyst was filtered and washed with alcohol. After complete removal of the solvent, followed by recrystallization of the dry residue from acetone, we obtained 21.8 g (45.7%) of 1-benzoyl-2-methyl-4-hydroxydecahydroquinoline with m.p. 133—134°, corresponding to the alcohol-base (XIII) with m.p. 157—158°, and not depressing the melting point when mixed with the above-described specimen. The remainder of the isomers (25.1 g) was saponified using a large excess of 10% hydrochloric acid, and here the saponification went very slowly and with much tar formation. After the heating, the benzoic acid was separated, the aqueous solution was evaporated to dryness, and the mixture of isomers was separated in the manner described above. We obtained 3.2 g of the hydrochloride of alcohol (XII) with m.p. 311—312°, and 4.8 g (16.2%) of alcohol (XIII) with m.p. 157—158°. The total yield of isomer (XIII) (m.p. 157—158°) from the hydrogenation was 61.9%.

Hydrogenation of the δ-isomer of 1-benzoyl-2-methyl-4-ketodecahydroquinoline (Vb). A solution of 20.0 g of the δ-isomer (Vb), m.p. 117—118°, in 160 ml of alcohol was hydrogenated on nickel catalyst, prepared from 10 g of the alloy, and previously saturated with hydrogen in 30 ml of alcohol. The calculated amount of hydrogen (1.95 liters) was absorbed after shaking for 3 hr. Another 20 g of ketone (Vb) was hydrogenated under the same conditions. The products from the two hydrogenations were separated from catalyst, and then were recrystallized from alcohol. We obtained 37.4 g (92.3%) of (XVI) with m.p. 182—183°, being the derivative of alcohol (XIV) with m.p. 114—115° (see below). The residue from the recrystallization weighed 1.4 g.

Found %: N 5.50, 5.36. $C_{17}H_{23}O_2N$. Calculated %: N 5.13.

Benzoylation of 1-benzoyl-2-methyl-4-hydroxydecahydroquinoline (XVI). A mixture of 40 g of (XVI), m.p. 182—183°, and 41 g of benzoyl chloride was heated for 20 min at 135—140° until the evolution of hydrogen chloride ceased. The excess benzoyl chloride was distilled off using a water-jet pump, while the crystalline residue was washed with ether and then recrystallized from alcohol. We obtained 22.7 g (50.2%) of the hydrochloride of the benzoate of 2-methyl-4-hydroxydecahydroquinoline (XVIII) with m.p. 303—305°.

Found %: N 4.87, 4.67. $C_{17}H_{24}O_2NCl$. Calculated %: N 4.52.

A solution of 16.7 g of the hydrochloride of benzoate (XVIII) in water was decomposed with aqueous sodium hydroxide solution. The free base was extracted with ether, then dried over sodium sulfate, and after removal of the solvent, it was recrystallized from acetone. We obtained 13.34 g of benzoate (XVIII) as tiny transparent plates with m.p. 75—76°.

Found %: C 74.68, 74.46; H 8.59, 8.39; N 5.57, 5.72. $C_{17}H_{23}O_2N$. Calculated %: C 74.66; H 8.48; N 5.12.

The picrate was obtained as fine needles with m.p. 216—217° (from alcohol).

Found %: C 54.98, 54.70; H 5.31, 5.83; N 11.23, 10.92. $C_{23}H_{26}O_9N_4$. Calculated %: C 54.97; H 5.21; N 11.15.

From the ether solution, obtained in washing the benzoate (XVIII) hydrochloride with m.p. 303—305°, after removal of the solvent and recrystallization of the residue from benzene, we obtained 13.3 g of benzoate (XVII) with m.p. 123—125°.

Found %: N 3.58, 3.77. $C_{24}H_{27}O_3N$. Calculated %: N 3.71.

Saponification of the benzoate of 2-methyl-4-hydroxydecahydroquinoline (XVIII). A mixture of 1.45 g of benzoate (XVIII), m.p. 75—76°, and 2.3 g of KOH in 77 ml of alcohol was refluxed for 1 hr. The cooled solution was acidified with hydrochloric acid, the potassium chloride was filtered, and the alcohol was distilled off under a slight vacuum, after which the residue was dissolved in water, and the solution washed with ether and then decomposed with potassium carbonate. The free base was extracted with ether, dried over sodium sulfate, and after removal of the ether, it was recrystallized from acetone. We obtained 0.84 g of isomer (XIV) with m.p. 114—115°.

Found %: C 71.34, 71.30; H 11.28. 11.18; N 0.05 8.09. $C_{10}H_{19}ON$. Calculated %: C 70.96; H 11.31; N 8.28.

The hydrochloride was obtained as clusters of plates with m.p. 278—279° (from alcohol by precipitation with ether).

Found %: N 6.85, 7.03. $C_{10}H_{20}ONCl$. Calculated %: N 6.81.

The picrate was obtained as fine needles with m.p. 160—161°.

Found %: N 13.82, 13.51. $C_{16}H_{22}O_8N_4$. Calculated %: N 14.06.

SUMMARY

A study was made of the reduction of the γ-isomer of 2-methyl-4-ketodecahydroquinoline, its benzoyl derivative, and the benzoyl derivative of the δ-isomer. Three of the four theoretically possible racemates of 2-methyl-4-hydroxydecahydroquinoline were obtained.

LITERATURE CITED

[1] D. V. Sokolov, G. S. Litvinenko, and K. I. Khludneva, J. Gen. Chem. 29, 1112 (1959).

[2] D. V. Sokolov, G. S. Litvinenko, and K. I. Khludneva, J. Gen. Chem. 29, 3204 (1959).*

[3] W. Klyne, Progress in Stereochemistry (London, 1954), Vol. 1, p. 36; I. N. Nazarov and L. D. Bergel'son, Prog. Chem. [USSR] 26, 3 (1957); D. R. Barton and R. C. Cookson, Quart. Rev. 10, 44 (1956); D. K. R. Chaudhuri and A. K. Rose, Science and Culture 19, 135 (1953); A. K. Rose and D. K. R. Chaudhuri, Nature 171, 652 (1953).

[4] R. Cornubert and J. Phelisse, Bull. soc. chim. France 399 (1952); C. A. 47, 4295 i.

* Original Russian pagination. See C. B. Translation.

A NEW METHOD OF SYNTHESIZING MACROCYCLIC COMPOUNDS

I. CYCLIZATION OF ω-THIENYLALKANOIC ACID CHLORIDES
TO MACROCYCLIC KETONES OF THE THIOPHENE SERIES
AND PREPARATION FROM THEM TO HIGHER CYCLOALKANONES

Ya. L. Gol'dfarb, S. Z. Taits, and L. I. Belen'kii

N. D. Zelinskii Institute of Organic Chemistry of the Academy of Sciences, USSR

The high reactivity of the thiophene ring, and especially of its α-positions, makes it comparatively easy to synthesize various thiophene derivatives from which aliphatic compounds of different types can be prepared by reductive desulfurization with Raney nickel [1-13]. In the present work it has been shown that the principle mentioned can be employed also for synthesis of many-membered alicyclic compounds.

The importance of some of the macrocyclic compounds, especially the ketones and lactones, as valuable perfume materials is well known. Recently the investigation of compounds with large, and particularly intermediate rings has provided interesting material for theoretical organic chemistry (cf., for example, [14]). We also should point out recent data indicating the unusual role of some macrocyclic compounds as carriers for important biological functions (cf., for example, [15]). In spite of the considerable success achieved in their synthesis as a result of the use of new methods, for example acyloin condensation [16], macrocyclic compounds are still not very readily available; this is in considerable degree due to the difficulty of obtaining the bifunctional derivatives necessary for cyclization.

Starting with thiophene, it is possible to arrive at such cyclic systems in two ways: 1) by the preparation from it of derivatives of bifunctional long-chain aliphatic compounds that can be closed to form macrocycles by methods already known (cf., for example, [4,5]); 2) by the synthesis of bi- or polycyclic compounds including thiophene rings and subsequent removal of the sulfur atoms, which play the role of a "bridge" in such systems [17]. The second path offers the possibility of utilizing the aromatic nature of the thiophene ring not only for the subsequent introduction of various substituents, which in case of necessity can be protected on hydrogenolysis, but also for accomplishing the cyclization process itself. In particular, in this work we employed intramolecular acylation by the Friedel-Krafts method, which yielded macrocyclic ketones of the thiophene series, which could then be converted to higher cycloalkanones. The application of this second route to the ketones that we had in mind is illustrated in Scheme 1.

It is easy to see that the ring with the maximum number of members (for a given length of chain introduced) is formed by process A, since in this case inclusion in the ring of all four carbon atoms belonging to the thiophene nucleus is guaranteed.

If we judge from the data in the literature, compounds of structure (I) had not been prepared until recently and only one macrocyclic compound of another type including two thiophene rings [18] had been described, and its structure was not indicated. On the contrary, for the benzene and naphthalene series a considerable number of systems are known that are similar or close to (I) and (II), having their first and fourth, or first and second carbon atoms of the aromatic nucleus connected with an aliphatic chain, which may carry a functional group. For the

---

*Here and below we have in mind thienyl-2.

Scheme 1

A. thiophene $\rightarrow$ $(CH_2)_n COCl$ $\rightarrow$ CO $(CH_2)_n$ (I) $\rightarrow$ $(CH_2)_{n+4}$ CO

Б. R-thiophene $\rightarrow$ R-$(CH_2)_n COCl$ $\rightarrow$ R CO $(CH_2)_n$ (II) $\rightarrow$ $R-CH_2-CH_2-CH$ CO $(CH_2)_n$ CH_2

В. R'-thiophene-R'' $\rightarrow$ R' $(CH_2)_n COCl$ R'' $\rightarrow$ R' CO $(CH_2)_n$ R'' $\rightarrow$ $R'-CH_2-CH$ $CO-(CH_2)_n$ $CH-CH_2-R''$

synthesis of such compounds various methods have been used, for example, pyrolysis of cerium salts of dicarboxylic acids [19], condensation of dinitriles [20], and acyloin condensation [21]. In addition, the Wurtz synthesis [22,23] and intramolecular acylation [24-26] have been employed. The yields from these reactions depend on the size of the cycles formed in the reaction, amounting to 20—70% in case of the formation of an 8-membered ring and rings with more than 14—16 atoms, including in this number 2 atoms of the benzene ring for ortho- and 4 for para-closing.

Compounds of type (II), in which n = 3 and 4, have been described by Fieser and Kennelly (n = 3, R = H) [27] and those with a 7-membered ring (n = 4, R = H or alkyl) by Cagniant and Cagniant [28], who synthesized * them in good yield by intramolecular acylation. The latter authors also succeeded in preparing a compound with an 8-membered ring (II, n = 5, R = C_2H_5) [29], but with only an 8% yield of the ketone. It is interesting to note that their attempts to synthesize a ketone with a 5-membered ring (II, n = 2, R = H) were unsuccessful [30] * * In the instances mentioned here carbon bisulfide was used as the solvent and stannic chloride as the condensing agent; use of aluminum chloride instead of the latter, it appears from the data of Cagniant and Cagniant [29], was impossible because of its destructive action on thiophene compounds.

For us, ketones of type (II) were of most interest in connection with our established goal. Considering the greater reactivity of the α-position of the thiophene ring in comparison with the β-position, it might be assumed that with the proper length of chain the closure on acylation (cf. Scheme 1) would go in the direction of the ketones represented by (I) and not (II). Success therefore depended on whether it was possible to limit intermolecular reaction. Having this fact in view, we decided to employ the method of acylation in benzene in the presence of stannic chloride [31] and to use an apparatus adapted to carrying out the process at high dilution and apply a small vacuum to lower the reaction temperature. The first experiments were set up with 6-thienylcaproic acid chloride. However, instead of the expected ketone (II, n = 5, R = H) we were able to isolate only a very insignificant amount of a product of reaction with two molecules of acid chloride, the diketone structure of which (III, n = 5) (cf. Scheme 2) follows from the fact that on hydrogenolysis of it the previously described cycloeicosanedione-1,11 (IV, n = 5) was obtained.

The lack of success in this case could be explained by the fact that stannic chloride, because of its volatility, was in the gaseous phase and elicited a reaction before the attainment of the necessary dilution; therefore, in the subsequent experiments it was replaced by aluminum chloride dissolved in sulfuric ether. The presence of the latter deactivated the $AlCl_3$ to some extent and also weakened its destructive action; we were able to satisfy ourselves of this by the example of the acylation of thiophene with the acid chloride of the monoethyl ester of adipic acid, which proceeded without appreciable tar formation. But even with such an experimental set-up, 9-thienylpelargonic acid chloride formed only an insignificant amount of the product of type (III) (n = 8). Under

_____
*However, not as starting materials for the preparation of alicyclic compounds.
* *Similar compounds of the benzene series with 5- and 8-membered rings are obtained in high yields [24]. Obviously the geometry of the thiophene ring differs essentially from that of benzene.

these same conditions 10-thienylcapric acid chloride gave the diketone (III, n = 9) in 17% yield. Similar dike-
tones, contrary to expectations, were obtained in somewhat better yields without the use of the high-dilution tech-
nique by cyclization in benzene with the aid of stannic chloride at 5°.

Scheme 2

By the action of Raney nickel on the above-mentioned diketones (III, n = 8 and 9) we obtained the corres-
ponding cyclohexacosanedione-1, 14 (IV, n = 8) and cyclooctacosanedione-1, 15 (IV, n = 9), thus establishing the
structures of the former two compounds. Supplementary confirmation of the structure of the cyclization product
of 10-thienylcapric acid was found in the fact that its reduction by the method of Kizhner and subsequent hydro-
genolysis of the reduction product (V) produced the previously described cyclooctacosane (VI). Hydrogenolysis
was carried out by heating with Raney nickel (2-3 hours at 30-50°) prepared according to [32], and employing as
the solvent in all cases a mixture of benzene and ethanol to which acetone was added if it was necessary to stop
the reaction at the stage of the formation of the cycloalkanone. Under such conditions the yields of the macrocy-
clic ketones, calculated on the basis of the thiophene ketones, amounted to 70−90%. It is known [33] that acetone
suppresses the reduction by Raney nickel of the carbonyl group to hydroxyl; however, as can be seen in our experi-
ments, an excess of acetone noticeably deactivates Raney nickel and may slow down the reaction.

It was of interest to find out which factor—the magnitude of the ring that
was formed or the comparative reactivity of the α-position of the ring—was of
predominant significance in reactions of ω-thienylalkanoic acid chlorides. In
other words, will intermolecular condensation (at the expense of α-hydrogen at-
oms) or intramolecular condensation (as a result of replacement of β-hydrogen
atoms) take place, if as a result of the latter process a more thermodynamically
advantageous 6- or 7-membered ring can be formed. To clarify this question
we studied the behavior of the acid chlorides of 4-thienylbutyric and 5-thienyl-
valeric acids under conditions similar to those mentioned. In this study we ob-
tained good yields of the previously described ketones (II, R = H, n = 3 and 4)
with 6- and 7-membered rings. • These data permit the statement that the be-
havior of the acid chlorides referred to under the conditions of the condensation
reaction is determined first of all by steric factors, and particularly depends on
the possibility of ring formation.

In the experiments described above, instead of products of intramolecular
ring closure of type (I) we obtained tricyclic compounds of type (III). Inasmuch,
however, as benzene analogs of systems of type (I) had been described by Huis-
gen [24], who synthesized them from the corresponding acid chloride in the heterogeneous system $AlCl_3$ −CS_2, it

To reflux
condenser

To Hershberg
funnel

To reaction
flask

---
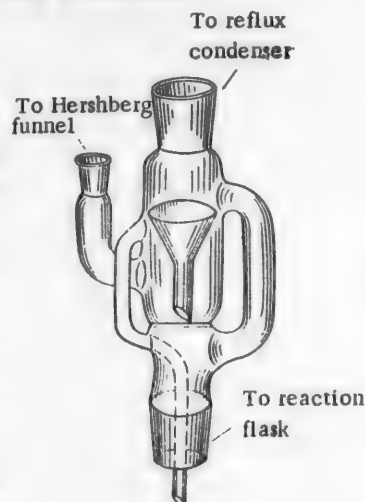
*It should be noted that thiophenocycloheptanone was obtained in our experiments in a yield 1.5 times higher than
that described in the literature [28].

seemed expedient to disregard the considerations stated by Cagniant and Cagniant [30] and to set up a similar experiment with one of the acid chlorides of the thiophene series that have been mentioned. Actually, when we cyclized 10-thienylcapric acid chloride under these conditions, we obtained the monoketone (I, n = 9) although the yield (13%) still was meager. By hydrogenolysis of this ketone we obtained the cyclotetradecanone (VII), thus confirming the structure of the former. Since in this last case acylation probably takes place on the surface of the solid $AlCl_3$, it seemed expedient to carry out the reaction in the presence of an agent with a well developed surface. Such a condensing agent was prepared by the gradual addition of an ether solution of $AlCl_3$ to boiling carbon bisulfide; when this was done, a very fine suspension separated out, and the acid chloride was added to this with the aid of a device depicted in the figure, which guaranteed conditions of high dilution.

In the experiment with 10-thienylcapric acid chloride a sharp increase in the yield (up to 70%) of the ketones (I, n = 9) and (III, n = 9) was attained at once, the yield calculated as the former amounting to 40%. This result indicates the value of such a cyclization technique for the preparation of macrocyclic compounds including a thiophene ring. In subsequent communications we will consider the problem of the specific properties of the condensing agent employed and the effect of the length of the carbon chain of the ω-thienylalkanoic acids on the character and yield of the products.

Nomenclature of macrocyclic compounds containing thiophene rings. The nomenclature of the bridged polycyclic systems to which the macrocycles of the thiophene series that we have prepared belong has been inadequately developed and sometimes leads to very complex names. For example, according to the Bayer-Patterson system the diketone (III, n = 5) prepared by us would be called 21,22-dithiatricyclo-(16, 2, 1, $1^{8,\ 11}$)-docosatetraene-8, 10, 18, 20-dione-2, 12. Therefore we propose to introduce a simplified nomenclature and by analogy with similar compounds of the benzene series [23, 26] to call materials in whose molecules the α-positions of one or several thiophene rings are joined with short polymethylene chains α-cyclothienes. Compounds in which the polymethylene chains are between β-positions or α- and β-positions will be called β-cyclothienes or α, β-cyclothienes, respectively. Before the name, in square brackets, will stand figures that show the number of methylene groups in each of the bridges, and in the name will be indicated the number of thiophene rings. Thus, the name of the product (V, n = 9) should be [10, 10]-α-cyclodithiene. A compound of structure (A) will be called (m-α, α; n-β, β')-cyclodithiene. If the cyclothiene is a dithienyl derivative, for example (B), then one of the figures will be O—[x, O]-α-cyclodithiene.
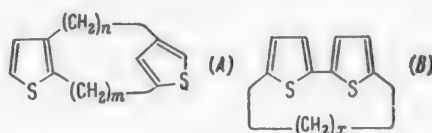
All of the carbon atoms are numbered in succession around the contour, starting with the end atom of the longest chain next to the least substituted thiophene ring.
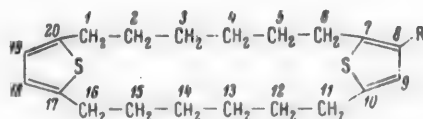
In the presence of substituents the name is formed according to the general rule; for example, the name of (III, n = 5) will be [6, 6]-α-cyclodithienedione-1, 11 and that of (I, n = 9) will be [10]-α-cyclothienone-1.

Synthesis of starting ω-thienylalkanoic acid chlorides was carried out according to the general scheme:

$$\underset{S}{\boxed{}} + ClCO(CH_2)_mCOOR \longrightarrow \underset{S}{\boxed{}} -CO(CH_2)_mCOOR \longrightarrow$$

$$\begin{array}{ll} m = 2, 3, & R = CH_3 \\ m = 4, 7, 8, & R = C_2H_5 \end{array} \qquad \text{(VIII)}$$

$$\longrightarrow \underset{S}{\boxed{}} -(CH_2)_{m+1}COOH \longrightarrow \underset{S}{\boxed{}} -(CH_2)_{m+1}COCl$$

$$\text{(IX)} \qquad\qquad\qquad\qquad \text{(X)}$$
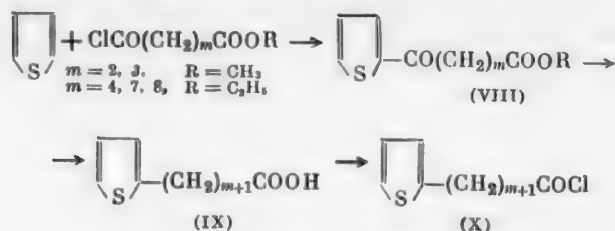
The methyl acid esters of succinic and glutaric acids were prepared by the action of methanol on the corresponding anhydrides; the ethyl acid esters of adipic, azelaic, and sebacic acids were prepared by transesterification by means of prolonged boiling of a mixture of the acid, its diethyl ester, and ethanol in the presence of hydrochloric acid [34]. By treatment of the acid esters with thionyl chloride the acid chlorides were obtained, which were then reacted with thiophene in benzene medium in the presence of stannic chloride at a temperature of about +5°, yielding on the order of 70% of the corresponding ketoesters. By reduction by the Kizhner method as modified by Huang-Minlon [35], the ketoesters were converted in yields above 90% (except for 4-thienylbutyric acid, where the yield was 81%) to the corresponding ω-thienylalkanoic acids, which were treated with thionyl chloride in absolute ether (cf. [27]) to obtain the acid chlorides. After the ether and excess thionyl chloride were removed, the acid chlorides were distilled and sometimes were used without further purification. The constants and yields of the starting materials prepared by us and the intermediate compounds are given in Tables 1-3.

Experiment on the intramolecular acylation of 6-thienylcaproic acid chloride in benzene in the presence of SnCl₄ and using a high dilution technique. The apparatus consisted of a two-liter, three-necked reaction flask fitted with a stirrer with a seal, a thermometer, and a reflux condenser, the latter connected at the top with a dropping funnel and a descending condenser set in a two-necked flask to the second neck of which was attached a vacuum line. 1 liter of dry, thiophene-free benzene was placed in the reaction flask and about 150 ml of it was distilled off to free the glass apparatus from traces of moisture. 39 g of stannic chloride was added to the flask with the aid of a water pump and a manostat that maintained a pressure of 75—80 mm in the apparatus, the benzene was brought to boiling (b.p. 23°), and a solution of 20.45 g of 6-thienylcaproic acid chloride in 700 ml of benzene was added slowly through the reflux condenser. Because of the presence of some stannic chloride in the benzene vapors, the reflux condenser was covered inside with a red film of complex. The solution gradually became red. Addition of the acid chloride took 31 hours. The reaction mixture was stirred for an hour more, after which about 650 ml of benzene was distilled off and the complex was decomposed with dilute (1:10) hydrochloric acid at a temperature not higher than +10°. 1250 ml of acid and 800 ml of benzene were added, but the product obtained after breakdown of the complex dissolved only partially in the benzene. After 11 hours of stirring at room temperature, the benzene-insoluble material (13.25 g) was separated off. From the benzene solution about 2 g of another product was separated. Upon treatment with ether, an ether-insoluble fraction was separated from it (about 1 g), by repeated crystallization of which from alcohol and dioxane 0.5 g of [6, 6]-α-cyclodithienedione-1, 11 was obtained with m.p. 141—142.5°.

Found %: C 66.74, 66.86; H 6.71, 6.83; S 17.34; 17.54; M (by Rast method) 350, 388. $C_{20}H_{24}O_2S_2$. Calculated %: C 66.60; H 6.74; S 17.78. M 360.54.

When the experiment was repeated but the acylation was carried out in ether with AlCl₃ (for method, see below) we were not able to isolate the compound with m.p. 141—142.5° in the pure state. As regards the ether-soluble fraction of the product, it contained mainly 6-thienylcaproic acid, which was obtained by hydrolysis of the unreacted acid chloride.

Intramolecular acylation in ether in the presence of AlCl₃. 1. Cyclization of 9-thienylpelargonic acid chloride. The apparatus for the cyclization consisted of a 3.5 liter three-necked flask fitted with a stirrer with a mercury seal, a thermometer, and a cap for carrying out the reaction under conditions of high dilution (see figure). To the cap were connected a reflux condenser and a Hershberg funnel for slow, uniform delivery [38], both of which were equipped with calcium chloride tubes. In the reaction flask was placed a solution of 17 g of anhydrous AlCl₃ in 1 liter of absolute ether, the ether was brought to boiling, and in the course of 28.5 hours 1 liter of an ether so-

TABLE 1

Esters of ω-Thienylalkanoic Acids (VIII)

(VIII) m	R	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Yield, calc. on thiophene (in %)	Literature data
2	CH₃	173—174° (15)	1.5433	—	67	B. p. 174° (16 mm), n_D^{20} 1.5437 [36]
3	CH₃	165—168 (7)	1.5373	—	72.5	B. p. 173° (11 mm), n_D^{20} 1.5377, d_4^{20} 1,1943 [36]
4	C₂H₅	163—166 (2)	1.5236	1.1354	67	B. p. 185-186° (12 mm), n_D^{20} 1.5236, d_4^{20} 1.1328 [36]
7	C₂H₅	181—182 (2)	1.5104	1.0767	71	B. p. 224.5-226° (10 mm), $n_D^{17.5}$ 1.5116, d_4^{19} 1.082 [30]
8	C₂H₅	184—185 (1)	1.5065	1.0618	63	B. p. 230° (12 mm); $n_D^{19.2}$ 1.5058 d_4^{25} 1.064 [37]

TABLE 2

ω-Thienylalkanoic Acids (IX)

(IX) m	Boiling point (mmHg)	Melting point	Yield, calc. on (VIII) (in%)	Literature data
2	172—174° (20)*	—	81	B. p. 168° (14.5 mm) n_D^{20} 1.5317 [36]
3	163—164 (9)	39—41°	96.5	B. p. 177° (14 mm), m.p. 41-43° [36]
4	—	41—41.5	93	B. p. 201° (19 mm), m.p. 40° [37]
7	—	35.5—36	94	B. p. 217° (10.2 mm), m.p. 35° [30]
8	171—173 (1)	33—33.8	94**	B. p. 222° (9.8 mm), m.p. 25.5° [30]

* n_D^{25} 1.5305.

** Found %: C 66.01, 65.98; H 8.67, 8.65; S 12.28, 12.34. C₁₄H₂₂O₂S. Calculated %: C 66.10; H 8.72; S 12.60. Neutr. equiv. 255.3; Calc. 254.39.

TABLE 3

ω-Thienylalkanoic Acid Chlorides (X)

(X) m	Boiling point (pressure in mm)	Yield, calc. on (IX) (in %)	Boiling point according to literature data
2	102—104° (0.7)	90.5	104—110° (2 mm) [27]
3	102—105 (0.7)	76.5	125 (4 mm) [28]
4	120—122 (0.5)	84*	147 (7.5 mm) [37]
7	142—146 (1)	87	165 (3.2 mm) [30]
8	163—165 (2)	92	Decomposes upon distillation [37]

* n_D^{20} 1.5234, d_4^{20} 1.1443, MR_D 57.90; Calc. 57.65.

TABLE 4

(X) m	Amount (in moles) (X)	Amount (in moles) SnCl₄	Reaction time (in hours)	Reaction product	Yield (in %)	Melting point	Boiling point (pressure in mm)	Found % C	Found % H	Found % S	Empirical formula	Calculated % C	Calculated % H	Calculated % S	Literature data
2	0.084	0.16	7.5	II, n = 3	92	34.5—35.5°	81—84° (0.3)	62.74, 62.74	5.51, 5.44	20.80, 21.02	C_8H_8OS	63.14	5.29	21.07	M.p. 35.5—37°, b.p. 104—110° (2 mm) [27]
3	0.042	0.16	6	II, n = 4	70	—	114.5—115.5 (3)*	64.64, 64.92	6.08, 5.94	19.47, 19.33	$C_9H_{10}OS$	65.02	6.06	19.29	B.p. 156° (13 mm), semicarbazone, m.p. 187° [28]
4	0.05	0.16	17	III, n = 5	8.3	142—143.5	—	66.63, 66.60	6.64, 6.68	17.64, 17.75	$C_{20}H_{24}O_2S_2$	66.60	6.74	17.78	—
7	0.05**	0.16**	13	III, n = 8***	3.6	82—83.5	—	—	—	—	—	—	—	—	—
8	0.05	0.08	6.5	III, n = 9****	15	101—102	—	—	—	—	—	—	—	—	—

*n_D^{20} 1.5875, d_4^{20} 1.2006. Semicarbazone, m.p. 187—188° (corr.); Found %: N 18.99, 19.17, $C_{10}H_{15}ON_3S$. Calculated %: N 18.82.

** In 750 ml of dry benzene.

*** Gave no depression in melting point with a sample of (III, n = 8) prepared by carrying out the reaction in ether with AlCl₃.
Found: M 429, 432, $C_{26}H_{36}O_2S_2$. Calculated: M 444.68.

**** Gave no depression in melting point with a sample of (III, n = 9) prepared by carrying out the reaction in ether with AlCl₃.

lution of the acid chloride prepared from 18 g of 9-thienylpelargonic acid was added through the Hershberg funnel. During this process the acid chloride solution was mixed with the condensate flowing from the reflux condenser and was continuously fed in dilute form through the surrounding tube into the reaction flask. At the end of the addition of the acid chloride the reaction mixture was treated with 50 ml of concentrated HCl in 500 ml of a mixture of finely crushed ice and water. The ether solution was separated from the aqueous layer and the polymer (the latter in the main remained on the walls of the flask) was washed with sodium carbonate solution, then with water, and was dried with magnesium sulfate. The weight of the residue after distillation of the ether was 0.93 g. After repeated crystallization from alcohol, 0.15 g (0.9%) of [9, 9]-α-cyclodithienedione-1, 14 was obtained with m.p. 82—83.5°. •

Found %: C 70.03, 69.96; H 8.29, 8.15; S 14.61, 14.46. $C_{26}H_{36}O_2S_2$. Calculated %: C 70.22; H 8.16; S 14.42.

2. **Cyclization of 10-thienylcapric acid chloride** was carried out in a manner similar to the preceding experiment. From 13 g of the acid was obtained about 1 g of [10,10]-α-cyclo-dithienedione-1,15 with m.p. 99.5—101° (from heptane). About half of the starting acid (about 6 g) was isolated unchanged. The yield of ketone based on the acid used was 17%.

Found %: C 70.84, 70.96; H 8.61, 8.55; S 13.37, 13.12. $C_{28}H_{40}O_2S_2$. Calculated %: C 71.13; H 8.53; S 13.57.

Cyclization of ω-thienylalkanoic acid chlorides in benzene in the presence of SnCl₄ without use of the high dilution technique. In a 4-necked flask fitted with a stirrer with seal, dropping funnel, calcium chloride tube, and thermometer, was placed a solution of stannic chloride (0.1—0.15 mole) in 500 ml of dry, thiophene-free benzene and a solution of the acid chloride (0.04—0.09 mole) in 500 ml of dry benzene was added slowly, drop by drop, while stirring and at a temperature of 4—6°. The mixture was stirred for 1 hour at room temperature and either left to stand overnight or immediately decomposed with 100 ml of dilute (1:10 by volume) hydrochloric acid, while the tempera-

*In a previous communication [17] a higher melting point was erroneously indicated.

TABLE 5

Starting compd. and amount (in g)	Amount				Reac-tion temp.	Reac-tion time (in hrs)	Product and its empirical formula	Yield (in %)	Melting point		Found %		Calculated %	
	Raney nickel (in g)	ben-zene (ml)	alco-hol (ml)	ace-tone (ml)					found	according to literature data	C	H	C	H
V, n = 9, 0.32	3	40	50	—	50°	3	VI, C₂₈H₅₈*	71	47.5-49°** (from a mixture of benzene and alcohol)	47-48° [39]	85.58, 85.87	14.30, 14.31	85.63	14.37
III, n = 5, 1.1	6	20	100	20	35	2	IV, n = 5, C₂₀H₃₆O₂	90***	48.5-50 ** (from alcohol)	48-51 [40], 49-51 [41]	77.56, 77.60	11.51, 11.67	77.85	11.76
III, n = 8, 0.5	5	20	80	20	35	2.5	IV, n = 8, C₂₆H₄₈O₂	63.5	67-68** (from alcohol)	68-69 [39]	79.33, 79.33	12.34, 12.37	79.53	12.12
III, n = 9, 0.5	3	20	40	40	30-40	13	IV, n = 9, C₂₈H₅₂O₂	68	71.5-72.5° (from methanol)	72-73 [39]	79.81, 79.53	12.47, 12.30	79.93	12.46
I, n = 9, 1.0	7	—	75	35	40	12	VII; C₁₄H₂₀O****	85*****	52.2-53° (from alcohol)	52-53 [39]	79.40, 79.39	12.20, 12.30	79.93	12.46

*M (by Rast method) 419, 421; Calc. 392.73.

** See note on p. 3533.

*** Yield based on unpurified product with m.p. 44-47°.

**** Semicarbazone, m.p. 202.5-203.5° (from alcohol or aqueous dioxane, corr.). Found %: C 67.44, 67.27; H 10.81, 10.90; N 15.89, 15.73. C₁₅H₂₆ON₃. Calculated %: C 67.37; H 10.93; N 15.72.

***** Yield based on unpurified product with m.p. 49-50°.

ture was kept not higher than +10°. The benzene layer was separated from the polymer, washed with water, sodium carbonate solution, and again with water, the benzene was removed, and the residue was either distilled or crystallized. The results of the experiments are given in Table 4.

Reduction of [10, 10]-α-cyclodithiene-dione-1, 15 (III, n = 9) by the Kizhner method. 0.9 g of uncrystallized diketone was dissolved with heating in 15 ml of diethylene glycol that contained 0.7 g of hydrazine hydrate. To the clear solution was added 0.73 g of potassium hydroxide; the mixture was refluxed for 4.5 hours at 150-170°, after which several drops of liquid were distilled off, and the temperature of the mixture was raised to 210-230°. Boiling was continued at this temperature for 5.5 hours. The mixture, after being cooled, was diluted twofold with water, extracted with ether, and the extract was washed with water and dried over calcium chloride. After the ether was distilled off, 0.73 g (81%) of unpurified [10, 10]-α-cyclodithiene was obtained in the form of yellowish-green crystals, m p. 51.5 -53.5° (from petroleum ether and methyl cellosolve).

Found %: C 75.54, 76.04; H 9.88, 9.98; S 14.64, 14.68. M 417, 446. C₂₈H₄₄S₂. Calculated %: C 75.60; H 9.97; S 14.42. M 444.70.

Intramolecular acylation of 10-thienyl-capric acid chloride in carbon bisulfide in the presence of aluminum chloride and using the high dilution technique was carried out in an apparatus similar to that used in carrying out the reaction in ether. In the flask of the apparatus was placed 1.4 liters of carbon bisulfide distilled over AlCl₃; 100 ml of this was then distilled off through the reflux condenser (without water) to dry the apparatus, 40 g of anhydrous AlCl₃ was then introduced into the flask, the carbon bisulfide was brought to boiling, and over the course of 61 hours a solution of 5.5 g of 10-thienylcapric acid chloride in 500 ml of carbon bisulfide was added through the cap. At the end of the addition of the acid chloride the mixture was boiled for 2 hours, then 1 liter of carbon bisulfide was distilled off, and the mixture was cooled to +10° and treated with 1 liter of dilute hydrochloric acid. The carbon bi-

sulfide layer, after separation of the insoluble polymer, was washed with water, sodium bicarbonate solution, and again with water and dried over magnesium sulfate. After the solvent was distilled off, 1.2 g of an oil was obtained that slowly crystallized on standing in a vacuum desiccator over alkali. When the oil was shaken with ether, crystals insoluble in ether were isolated (0.1 g, m.p. 99—101°, gave no depression in melting point when mixed with a sample of the previously prepared III, n = 9). The residue after evaporation of the ether crystallized on prolonged standing. After these crystals were pressed out on a porous plate, 0.6 g (12.5%) of [10]-α-cyclothienone-1 (I, n = 9) was obtained with m.p. 35.5—37.5°. A sample for analysis, prepared by crystallization from hexane, melted at 35-35.5°.

Found %: C 70.66, 70.64; H 8.43, 8.54; S 13.46, 13.46. M 232, 235. $C_{14}H_{20}OS$. Calculated %: C 71.13; H 8.53; S 13.57. M 236.37.

Oxime, m.p. 133—134.5° (from aqueous methanol).

Found %: N 5.31, 5.43. $C_{14}H_{21}ONS$. Calculated %: N 5.37.

Intramolecular acylation of 10-thienylcapric acid chloride in the presence of finely divided $AlCl_3$. In the reaction flask was placed 1750 ml of carbon bisulfide, and after 100 ml had been distilled off, 15 g of $AlCl_3$ in 25 ml of ether was added, then parallel with the addition of the acid chloride to the reaction mixture 75 ml of a solution of 75 g of $AlCl_3$ in 130 ml of ether was continuously introduced drop by drop. A solution of 16.5 g of the acid chloride in 700 ml of carbon bisulfide was added over the course of 60 hours. After the usual treatment of the reaction mixture, a residue was obtained consisting of about 11 g of a neutral substance from which 3.4 g (31.4%) of the diketone (III, n = 9) with m.p. 100—101° was isolated by shaking with ether. The ether solution was evaporated and the residue slowly crystallized on standing. After it was pressed out on a porous plate, 3 g of [10]--α-cyclothienone-1 with m.p. 128.5—132° was obtained (yield of oxime and its melting point are shown for the material recrystallized from aqueous alcohol). Thus, the yield of monoketone (I, n = 9) amounted to 40.6%. In other experiments the [10]-α-cyclothienone-1 was isolated by distillation; b.p. 149—152° (1 mm).

Reductive desulfurization of macrocyclic compounds containing thiophene rings. A solution of the thiophene compound in a mixture of benzene and alcohol (and acetone in the case of ketones) was stirred at 30—50° with Raney nickel until there was a negative reaction for sulfur with sodium nitroprusside. The nickel was filtered off, the solvent was evaporated, and the residue was crystallized. The results of the experiments are given in Table 5.

SUMMARY

1. By the use of intramolecular acylation of ω-thienylalkanoic acid chlorides a series of macrocyclic compounds that included thiophene rings was prepared. The best results, adaptable to preparative use, were obtained by using a finely dispersed condensing agent that was produced by special treatment of aluminum chloride.

2. A new method was developed for the preparation of many-membered cycloaliphatic compounds, comprising the reductive desulfurization of the appropriate macrocycles including thiophene rings.

LITERATURE CITED

[1] Ya. L. Gol'dfarb and M. S. Kondakova, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1952, 1131; Ya. L. Gol'dfarb and I. S. Korsakova, Proc. Acad. Sci. USSR, 96, 283 (1954).

[2] F. F. Blicke, D. G. Sheets, J. Am. Chem. Soc. 70, 3768 (1948); 71, 4010 (1949).

[3] D. Papa, E. Schwenk, H. Ginsberg, J. Org. Ch. 14, 723 (1949).

[4] Ya. L. Gol'dfarb and M. L. Kirmalova, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1955, 570.*

[5] N. P. Buu-Hoi, M. Sy, N. Dat-Xuong, C. r. 240, 442 (1955).

[6] Ya. L. Gol'dfarb and M. L. Kirmalova, J. Gen. Chem. 25, 1373 (1955).*

[7] Ya. L. Gol'dfarb and P. A. Konstantinov, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1956, 992.*

[8] H. Wynberg, A. Logothetis, J. Am. Chem. Soc. 78, 1958 (1956).

[9] Ya. L. Gol'dfarb and P. A. Konstantinov, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1959, 121.*

*Original Russian pagination. See C. B. Translation.

[10] Ya. L. Gol'dfarb and P. A. Konstantinov, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1957, 217.*

[11] Ya. L. Gol'dfarb and M. B. Ibragimova, Proc. Acad Sci. USSR 106, 469 (1956).*

[12] Ya. L. Gol'dfarb and M. B. Ibragimova, Proc. Acad. Sci. USSR 113, 594 (1957).*

[13] Ya. L. Gol'dfarb and B. P. Fabrichnyi, Proc. Acad. Sci. USSR 100, 461 (1955); Ya. L. Gol'dfarb, B. P. Fabrichnyi, and I. F. Shalavina, Proc. Acad. Sci. USSR 109, 305 (1956);* J. Gen. Chem. 29, 891 (1959).*

[14] V. Prelog, in the book: Perspectives in Organic Chemistry . N. Y. 96—133 (1956); R. Huisgen, Angew. Chem., 69, 341 (1957); Ya. L. Gol'dfarb and L. I. Belen'kii, Prog. Chem., 26, 362 (1957).

[15] R. Adams, M. Gianturco, Angew. Chem. 69, 5 (1957); R. B. Woodward, Angew. Chem. 69, 50 (1957); V. du Vigneaud, C. Ressler, J. W. Swan, C. W. Roberts, P. G. Katsoyannis, J. Am. Chem. Soc. 76, 3115 (1954); R. Schwyzer, P. Sieber, Helv. Chim. Acta 40, 624 (1957).

[16] U.S. Patent 2228268; C. A. 35, 2534 (1941); V. Prelog, L. Frenkiel, M. Kobelt, P. Barman, Helv. Chim. Acta 30, 1741 (1947); M. Stoll, J. Hulstkamp, Helv. Chim. Acta 30, 1815 (1947).

[17] Ya. L. Gol'dfarb, S. Z. Taits, and L. I. Belen'kii, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1957, 1262.*

[18] W. Steinkopf, R. Leitsmann, K. Hoffmann, Lieb. Ann. 546, 188 (1941).

[19] L. Ruzicka, J. B. Buijs, M. Stoll, Helv. Chim. Acta, 15, 220 (1932).

[20] K. Ziegler, A. Lüttringhaus, Lieb. Ann. 511, 1 (1934).

[21] R. Kelly, D. M. McDonald, K. Wiesner, Nature 166, 225 (1950).

[22] W. Baker, J. F. McOmie, J. M. Norman, J. Chem. Soc., 1951, 1114; W. Baker, F. Glockling, J. F. W. McOmie, J. Chem. Soc., 1951, 1118.

[23] D. J. Cram, H. Steinberg, J. Am. Chem. Soc. 73, 5691 (1951).

[24] R. Huisgen, W. Rapp, Ber. 85, 826 (1952); R. Huisgen, W. Rapp, I. Ugi, H. Walz, J. Glogger, Lieb. Ann. 586, 52 (1954); R. Huisgen, V. Vossius, Monatsh. 88, 517 (1957).

[25] G. D. Hedden, W. G. Brown, J. Am. Chem. Soc. 75, 3744 (1953).

[26] W. M. Schubert, W. A. Sweeney, H. K. Latourette, J. Am. Chem. Soc. 76, 5462 (1954).   .

[27] L. Fieser, M. Kennelly, J. Am. Chem. Soc. 57, 1611 (1935).

[28] P. Cagniant, D. Cagniant, Bull. Soc. Chim., 1955, 680.

[29] P. Cagniant, D. Cagniant, Bull. Soc. Chim., 1956, 1152.

[30] P. Cagniant, D. Cagniant, Bull. Soc. Chim., 1954, 1349.

[31] G. Stadnikov, J. Goldfarb, Ber. 61, 2341 (1928).

[32] Synth. Org. Prep., Coll. 4, 349 (1953). **

[33] G. Spero, A. McIntosh jr., R. Levin, J. Am. Chem. Soc. 70, 1907 (1948); A. McIntosh jr., A. Searcy, E. Meinzer, R. Levin, ibid., 71, 3317 (1949); A. T. Blomquist, J. Prager, J. Wolinsky, ibid., 77, 1804 (1955).

[34] Synth. Org. Prep., Coll. 2, 345 (1949);* G. B. Brown, B. R. Baker and others , J. Org. Ch. 12, 160 (1947).

[35] Huang-Minlon, J. Am. Chem. Soc. 68, 2487 (1946); 71, 3301 (1949).

[36] B. P. Fabrichnyi, I. F. Shalavina, and Ya. L. Gol'dfarb, J. Gen. Chem. 28, 2520 (1958). *

[37] P. Cagniant, D. Cagniant, A. Deluzarche, Bull. Soc. Chim. 1948, 1083.

[38] Synth. Org. Prep., Coll. 2, 550 (1949). **

[39] L. Ruzicka, M. Stoll, H. W. Huyser, H. A. Boekenoogen, Helv. Chim. Acta 13, 1152 (1930).

[40] U.S. Patent 2584664; C. A. 46, 8675 (1952).

[41] L. Ruzicka, H. Schinz, Helv. Chim. Acta 11, 670 (1928); C. A. 22, 4483 (1928).

INVESTIGATION IN THE FIELD OF VAPOR-PHASE CATALYTIC HYDRATION

OF ACETYLENE AND ITS DERIVATIVES.

VI. STUDY OF REACTION BETWEEN ACETYLENE AND ALCOHOLS OVER SOLID CATALYSTS

Yu. A. Gorin and A. E. Kalaus

In previous work [1] a study was made of the processes of addition of water to acetylene and some of its derivatives under the influence of solid ionic catalysts—phosphates of cadmium, zinc, and copper—and ideas of a possible mechanism for these reactions were developed. The object of the present investigation was to study the reaction of acetylene with alcohols in the gaseous phase (also over solid catalysts) for the purpose of determining the possibility of synthesis by such a method of vinyl ethers, and of obtaining data that might broaden our ideas of the mechanism of vapor-phase catalytic hydration of acetylene to acetaldehyde. We started with the assumption that there should be a great similarity between the reactions of addition of alcohols and of water in the vapor phase to acetylene and that these conversions are accomplished by an analogous mechanism.

The addition of water to acetylene may in an intermediate stage proceed through vinyl alcohol, $CH_2=CHOH$ (addition of one molecule), which then quickly isomerizes to the aldehyde, or by way of the formation of an unstable, unsymmetrical bivalent alcohol $CH_3-CH(OH)_2$ (addition of two molecules), which further splits out a molecule of water and goes to acetaldehyde. In connection with the fact that vinyl alcohol and the bivalent alcohol with two hydroxyls on one carbon atom have not been isolated in the free state, proof of one or the other variant does not seem possible.

Similarly the addition of alcohols to acetylene may be represented by the scheme:

$$CH\equiv CH + ROH \longrightarrow CH_2=CHOR; \quad CH_2=CHOR + ROH \longrightarrow CH_3-CH(OR)_2.$$

The vinyl ethers and acetals that are formed by the addition to acetylene of one or two molecules of alcohol are completely stable compounds and their determination and identification does not cause any difficulty.

According to patent data, the reaction of alcohols with acetylene can be carried out in the vapor phase by passing the reactants over heated catalysts, zinc or cadmium salts of organic acids supported on carbon or pumice. There also are indications that soda lime, calcium oxide, or carbon impregnated with KOH [2] can be employed as catalysts for these processes.

We prepared and tested some of the catalysts mentioned (zinc acetate on activated carbon and on silica gel and KOH on carbon) for obtaining vinyl ethers from acetylene and ethyl alcohol, but did not obtain positive results; the maximum yield of vinyl ethyl ether was 7—8% calculated on the acetylene that reacted. Zinc phosphate with a small amount of copper (0.8%) added proved ineffective as a catalyst, since it caused intensive dehydration of the alcohol with the formation of ethylene.

Positive results were obtained with the catalytic zinc oxide, prepared by calcining zinc, proposed by us for the indicated reactions [3]. Using this catalyst we obtained from binary mixtures of acetylene with ethyl, butyl, and primary isoamyl alcohol as the primary reaction products high yields of the corresponding vinyl ethyl, vinyl butyl, and vinyl isoamyl ethers. It should be noted that zinc oxide also is a catalyst for the hydration of acetylene to aldehyde [4].

As a result of a study of the effect of various factors (molar ratio acetylene: alcohol, temperature, and volume velocity of acetylene) we selected the optimum conditions for the formation of the above-mentioned

TABLE 1*

Name of alcohol**		Temp. of expt.	Velocity C_2H_2, liter·hr/liter cat.	Conversion of acetylene (in %)	Yield of vinyl ethers calc. on acetylene (in mole %)	
					passed through	reacted
Ethyl	. . . . . .	310°	130	49	25	51
n-Butyl	. . . . .	320	130	39	28	72
Isoamyl	. . . . .	320	270	46	25	64
Water . . .		310	130	25	Yields of aldehyde	
					13	56

* Average data from two experiments.

** Molar ratio acetylene-alcohol 1:3;

ethers. Some of the most essential results of the experiments are given in Table 1. There also are given, for comparison, data obtained with the same catalyst in the hydration of acetylene to acetaldehyde. In the figure are shown curves for relation of the process of formation of the vinyl ethers to the degree of conversion of acetylene (the latter was changed by varying the volume velocity of the mixture of acetylene and alcohol). From the course of the curves it can be seen that when the degree of conversion of the acetylene was decreased (increase in the volume velocity of the mixture), the yields of vinyl ethers based on reacted acetylene increased. Thus, the vinyl ethers are the primary reaction products of acetylene and the alcohols.

Along with its ability to split out hydrogen from alcohol, zinc oxide also has weak dehydrating properties [5]. Therefore dehydrogenation and dehydration of the starting alcohols take place to some extent together with the formation of the vinyl ethers. The dehydration reaction is very undesirable, since the water evolved promotes partial hydrolysis of the ether and formation of aldehyde. Apparently for this reason, when the degree of conversion of the acetylene is increased (decrease in the volume velocity of the mixture), the yield of aldehyde increases at the expense of hydrolysis of the vinyl ethyl ether (see figures 1, 3). It has been shown that addition of water to the mixture of acetylene and ethyl alcohol decreases the yield of vinyl ethyl ether and increases the yield of aldehyde as a result of hydrolysis of the ether. Vinyl ethyl ether alone at 310° over zinc oxide breaks down to the extent of 14.8%, and vinyl butyl ether to the extent of 7.0%. Dilution of these ethers with water (1:6 and 1:4) under the same conditions results in their hydrolysis to the extent of 79 and 71%, respectively.

In experiments on the preparation of ethers from mixtures of acetylene with alcohols, besides the side reactions of hydrolysis of the vinyl ethers and dehydrogenation and dehydration of the alcohols, we also observed the formation of some esters, probably by ester condensation of the aldehydes. When the temperature of the experiment was increased (up to 360°), there was a fall in the yield of vinyl ethyl ether based on reacted acetylene.

Furthermore, an increase in the temperature caused the formation of a small amount of acetone, which was not obtained under the optimum reaction conditions (310—320°). Acetals were not found in the reaction products of acetylene and the alcohols in any instance. It should be noted that diethyl acetal and dibutyl acetal passed over zinc oxide at 310—320° at the same volume velocity as the mixture of acetylene and alcohols broke down only to the extent of 50—65%. Thus, the acetals are stable enough under the conditions of the process studied, and if they were formed, they would be detected in the reaction products.

According to the ideas developed by us in previous communications [1], the hydration of acetylene over solid ionic catalysts is accomplished by the reaction of the acetylene with the cation of the catalyst lattice and the formation of a polar complex on the surface. By analogy with the scheme for the hydration of acetylene, the reaction between acetylene and the alcohols under the influence of a solid ionic catalyst, such as zinc oxide, can be expressed in the following fashion:

$$Zn^+ + CH{\equiv}CH \rightarrow Zn...CH{=}CH^{\delta+} \xrightarrow{C_2H_5OH} Zn^+ + CH_2{=}CH{-}OC_2H_5.$$
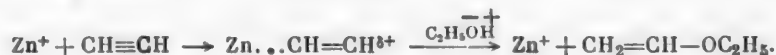
It is very probable that the zinc oxide influences the process not only as a catalyst that activates the acetylene, but also as an agent to increase the degree of polarization of the alcohol and promote its reaction with the polar acetylene complex. The formation of the vinyl ethers as the primary reaction products from acetylene and the alcohols over zinc oxide may serve as a basis for the idea that vinyl alcohol is an intermediate stage in the process of hydration of acetylene to acetaldehyde under the influence of solid catalysts.

<div align="center">EXPERIMENTAL</div>

The acetylene was first purified of contaminants by passing it through a solution of sodium hypochlorite. Rectified ethyl alcohol was freed of water over CaO and contained 99. 5% alcohol, b.p. 78°; n-butyl alcohol, b.p. 117.5—118°, d_4^{20} 0.8130; isoamyl alcohol (primary), b.p. 129—130°, $d_4^{20} =$ 0.8109; diethyl acetal, b.p. 101—102°, d_4^{20} 0.8295 was prepared by the method of Adkins [6]; dibutyl acetal, b.p. 184—185°, d_4^{20} 0.8321 was prepared by the method of [7]; vinyl ethyl ether, b.p. 36°, d_4^{20} 0.7537, and vinyl butyl ether, b.p. 93—94°, d_4^{20} 0.7795, were prepared by the method of [8]. The zinc oxide used as the catalyst was technical, brand M—1 (obtained by oxidation of metallic zinc at ~ 1300°).

The experiments were carried out in a vertical quartz tube (length 88 cm, diameter 28 mm) placed in an electric furnace. A section of the furnace at constant temperature was loaded with 50 ml of catalyst formed into "worms" with a size of ~3 mm. The reaction temperature was measured with a thermocouple placed in the center of the catalyst layer. The upper part of the furnace was filled with fragments of quartz and served as a vaporizer and preheater for the materials entering onto the catalyst. The liquid components were fed to the furnace from a buret. The purified acetylene was passed into a graduated gasometer, and thence entered through a rheometer into the reaction tube. The reaction products after leaving the furnace passed through a condenser and were collected in a vessel cooled with a mixture of ice and salt, and the gas after passing through a solution of hydroxylamine hydrochloride to trap vapors of aldehyde or vinyl ether was collected in a gasometer over a saturated solution of table salt.

The aldehyde was determined in the liquid reaction products by the method of [9]. The unsaturated compounds (vinyl ethers) were determined iodometrically after treatment of a sample of the condensate with a solution of bromine in CCl_4, and acetone was determined by means of furfurol by the method of [10]. The total of all the carbonyl compounds was determined with hydroxylamine hydrochloride, ethyl alcohol was determined by esterification with formic acid in the presence of sulfuric acid, butyl and isoamyl alcohols by acetylation with acetic anhydride in the presence of pyridine, acidity (calculated as acetic acid) by titration with 0.1 N alkali solution in the presence of phenolphthalein, and esters by saponification with 0.1 N alkali solution while heating on a water bath for 1 hour. Excess alkali was titrated with 0.1 N acid solution.

The general course of the analysis of the condensate obtained from an experiment was as follows. In a separate sample the sum of the carbonyl compounds, consisting of aldehyde and acetone (taking into account the aldehyde formed by hydrolysis of the vinyl ether and acetone), was determined with hydroxylamine. In other samples of the condensate under investigation, the aldehyde, acetone, and vinyl ether were determined by the methods indicated above. After appropriate recalculation for the carbonyl group, the difference between the total of the carbonyl compounds and the $=$ CO group entering into the vinyl ether, acetone, and aldehyde was ta-

Relation of formation of vinyl ethyl and vinyl butyl ethers from binary mixtures of acetylene and alcohols to conversion of acetylene (ratio C_2H_2: alcohol = 1:3 moles).

I. Experiments with acetylene—ethyl alcohol mixtures (310°): 1) Yield of ether based on C_2H_2 reacted; 2) yield based on C_2H_2 passed through; 3) yield of acetaldehyde from hydrolysis of ether, calculated on acetylene reacted. •

II. Experiments with acetylene—butyl alcohol mixtures (320°): 4) Yield of ether based on C_2H_2 reacted; 5) yield of ether based on C_2H_2 passed through.

* Yield of aldehyde from hydrolysis of ether was calculated as the difference between the total amount of acetaldehyde formed and the aldehyde obtained in a separate experiment where ethyl alcohol was passed over zinc oxide under the same conditions.

3538

ken by us as acetals. The alcohol and esters were determined in separate samples of the condensate. The methods indicated were verified on artificial mixtures and gave completely satisfactory results. The gaseous products were analyzed by absorption methods in an Orsat apparatus, hydrogen by combustion over palladized asbestos.

The vinyl ethers were isolated from the reaction products by rectification and purification from admixtures of aldehyde, alcohols, and water by heating with concentrated KOH and boiling over metallic sodium (Table 2).

According to the analysis with hydroxylamine hydrochloride, the vinyl ethyl ether isolated contained 98.8% ether, the vinyl butyl ether 98.2%, and the vinyl isoamyl ether 97.2%.

TABLE 2

Name of vinyl ether	Properties of ethers obtained from mixtures of acetylene and alcohols in vapor phase on zinc oxide			Literature data [8]		
	boiling point	d_4^{20}	n_D^{20}	boiling point	d_4^{20}	n_D^{20}
Vinyl ethyl	35.8—36.0°	0.7508	1.3770	36—36.1, 34.5—35.5°	0.7531, 0.7590	1.3779, 1.3778
Vinyl butyl	93.5—94.0	0.7790	1.4021	93.7—93.8, 93.3°	0.7792, 0.7788	1.4026, 1.4029
Vinyl isoamyl	111.2—111.5	0.7817	1.4085	112.5—112.8, 109—110°	0.7824, 0.7833	1.4098, 1.4070

SUMMARY

1. A catalyst, technical zinc oxide, has been proposed for the preparation of vinyl ethers from binary mixtures of acetylene and alcohols in the gaseous phase at 310—320°. The vinyl ethyl, vinyl butyl, and vinyl isoamyl ethers were prepared by this method and identified.

2. It has been shown that the vinyl ethers are the primary products of the reaction of acetylene with alcohols. The acetals are not obtained in this reaction.

3. The similarity between the vapor phase catalytic hydration of acetylene to aldehyde and the formation of vinyl ethers by the reaction of acetylene with alcohols over solid catalysts provides a basis for considering that the process of hydration of acetylene proceeds in an intermediate phase through the formation of vinyl alcohol, which further isomerizes to acetaldehyde.

4. Ideas have been stated concerning the mechanism of the formation of the vinyl ethers from acetylene and alcohols under the influence of solid ionic catalysts by the development of a polar complex of acetylene with the cation of the catalyst lattice and the addition to it of the polarized alcohol molecule.

LITERATURE CITED

[1] Yu. A. Gorin and L. P. Bogdanova, J. Gen. Chem. 28, 1144 (1958);* Yu. A. Gorin and I. K. Gorn, J. Gen. Chem 28, 2328 (1958).*

[2] Amer. Patent 2017355 (1935), Engl. Patent 430590, Chem. Abs. 29, 8001 (1935); Swed. Patent 82550 (1934); Zbl. 1936, II, 3846; W. E. Hanford, D. L. Fuller, Ind. Eng. Chem. 40, 1171 (1948).

[3] Yu. A. Gorin, A. E. Kalaus, and A. N. Makashina, USSR Patent, 12990 (1950); A. E. Kalaus, Diss., Study of the Reaction between Acetylene and Alcohols in the Vapor Phase over Solid Catalysts , VNIISK (1950).*

[4] T. Sakaki, J. Chem. Soc. Japan 67, 117 (1946).

[5] P. Sabatier, Catalysis in Organic Chemistry, State Chem. Tech. Press. 174 (1932).**

[6] Synthesis Org. Prep. 1, 62 (1949).**

[7] M. F. Shostakovskii and H. A. Gershtein, J. Gen. Chem 16, 937 (1946).

*Original Russian pagination. See C. B. Translation.
** In Russian.

[8] A. E. Favorskii and M. F. Shostakovskii, J. Gen. Chem. 13, 1 (1943); M. F. Shostakovskii, Simple Vinyl Ethers, Acad. Sci. USSR Press, 32 (1952).*

[9] W. Ponndorf, Ber. 64, 1913 (1931).

[10] V. V. Chelintsev and E. K. Nikitin, J. Gen. Chem. 3, 319 (1933).

* In Russian.

ALKYLATION OVER AN ALUMINOSILICATE CATALYST
ACTIVATED WITH GASEOUS HYDROGEN CHLORIDE

II. ALKYLATION OF PHENOL WITH ISOPROPYL CHLORIDE

I. F. Radzevenchuk

Leningrad Agricultural Institute

Recently the alkylphenols have gained industrial significance as surface-active agents, raw materials for the preparation of plastics [1], and additives for lubrication oils [2]. Some derivatives of the alkylphenols are good insecticides and fungicides [3]. However, the synthesis of the alkylphenols is difficult. Reports of research on the alkylation of phenol with tertiary alkyl halides [4] and with benzyl chloride [5] are found; but indications of successful alkylation with primary and secondary alkyl halides are lacking. The reaction goes slowly and requires the use of an equimolecular quantity of aluminum chloride [6].

In the present work we carried out the alkylation of phenol with isopropyl chloride at 70—130° in the presence of gumbrin that had been dried at 160° and was activated with gaseous hydrogen chloride. This catalyst has been used successfully by us for the alkylation of benzene with alkyl halides [7]. The isopropylphenols were obtained in 56% yield based on the isopropyl chloride taken for the reaction; the o-isopropylphenol was predominantly formed, with a small amount of p-isopropylphenol. It was established by a series of experiments that an active catalyst was obtained by passing hydrogen chloride through dry gumbrin in the environment of the reactants for 30 minutes at 25—45°. To determine whether the activation of the gumbrin by the gaseous hydrogen chloride was not connected with the formation of aluminum chloride, we carried out special experiments. However, aluminum chloride was not detected in the reaction medium. An attempt also was made to carry out the alkylation reaction with carefully dried silica gel in the presence of gaseous hydrogen chloride; isopropylphenols were obtained in insignificant yield in this case. The mechanism of the alkylation reaction in the presence of gumbrin and gaseous hydrogen chloride differs from the mechanism of alkylation in the presence of aluminum chloride It is known that when phenol is alkylated in the presence of $AlCl_3$, up to 23% phenol ethers are formed. The authors consider that in the first stage of the reaction the ethers are formed, which under the influence of the aluminum chloride and heating rearrange to alkylphenols [6]. In all the alkylation experiments under the conditions used by us, even those at 80°, phenol ethers were formed in very insignificant amount (1—2%). Although the presence of acid facilitates rearrangement of the ethers to alkylphenols [8], with gumbrin (under our conditions), evidently the reaction of direct alkylation of the benzene ring predominates [9].

It should be noted that when the reaction products were distilled, a fraction was obtained in small amount with b.p. 68—72°, n_D^{20} 1.4120, which gave a reaction for a double bond. This product was not investigated further.

EXPERIMENTAL

The purpose of the work was to prepare alkylphenols, therefore phenol was used in excess—2 moles of phenol to 1 mole of isopropyl chloride. Gumbrin was used to the extent of 25—50% the weight of the reactants. When the amount of gumbrin was decreased to 10%, the time for the reaction increased. The alkylation was carried out at 80—125°, with vigorous stirring, for 2.5 hours. The reaction goes even at 80°, but the duration is increased to 15 hours. The gumbrin should be dried at 160—170° to constant weight, since the presence in the reaction mixture of trifling amounts of water greatly lowers the yield of alkylphenols.

In a three-necked flask fitted with a reflux condenser, stirrer, and delivery tube for hydrogen chloride, was placed a mixture of phenol, half of the isopropyl chloride, and the freshly dried gumbrin, and the mixture was

heated slightly. At 25° a current of dry hydrogen chloride was passed through it. The temperature of the bath was gradually (in the course of 45 minutes) brought up to 70°, after which the current of hydrogen chloride was stopped and the heat was turned off. At room temperature the remaining isopropyl chloride was added dropwise over a period of 30—40 minutes with vigorous stirring. Then the reaction mixture was heated for 1 hour at 70—80° and 1 hour at 80—100°. When the bath temperature reached 130°, the heat was turned off. The course of the alkylation reaction was marked by the evolution of hydrogen chloride.

After the reaction ended, the contents of the flask were diluted with sulfuric ether and the gumbrin was filtered off and washed with ether. In the first experiments the filtrate was extracted with alkali to separate the phenol ethers from the alkylphenols. Because of the small amounts of ethers, the separation was poor and later the filtrate was simply washed with water, dried, and distilled. The alkylphenol fractions with b.p. 190—230° were obtained in 56% yield, calculated on isopropyl chloride. The phenol ethers were isolated in amounts of 1-2% They were liquid, b.p. 176-178°, n_D^{18} 1.5325, did not solidify at 0°, and possibly consisted mainly of the isopropyl ether of phenol. •

The alkylphenol fractions were distilled. All six of the fractions obtained gave a blue-green color with alcoholic $FeCl_3$ solution. The first fraction separated crystals at 0° with m.p. 25°. The constants and yields of the fractions in percent are given in the table. These fractions were a mixture of isomeric isopropylphenols with the first fractions (up to 220°) predominantly o-isopropylphenol, and the subsequent ones predominantly p-isopropylphenol. The separate isomers were isolated from these fractions by chromatography. In the literature there is information on the separation of the isomers of nitrophenol by means of chromatography [10]. The isopropylphenol fractions were dissolved in benzene and passed through a column with aluminum oxide. Elution was carried out with benzene, then alcohol and sulfuric ether. Since the isopropylphenols did not give colored adsorption zones on the aluminum oxide, equal volumes of the solvents were taken off. The isopropylphenols were very firmly held by the aluminum oxide and passed into solution with difficulty. However, two main fractions were isolated. The 1st was o-isopropylphenol – b.p. 212-214°, n_D^{20} 1.5270. The boiling point of the glycol ethers was 130°. At 0° the fraction solidified. The crystals melted at +10°. • •

The second fraction was p-isopropylphenol, which solidified on cooling. The white prismatic crystals had the constants m.p. 61°, b.p. 228°, glycol ethers m.p. 80°, which agreed with the literature data. Thus, o- and p-isopropylphenols were isolated by means of chromatographic analysis, with very great losses, it is true.

In order to determine whether aluminum chloride was formed in the alkylation, two parallel experiments were carried out with dried and undried gumbrin. In the latter instance the alkylation reaction did not go. The reaction liquids in both experiments were carefully separated from the gumbrin, evaporated on a water bath, their organic fraction was treated with aqua regia, and Al_2O_3, SiO_2, and Fe_2O_3 were determined qualitatively and quantitatively [11]. In both experiments only traces of Al_2O_3 and SiO_2 were detected. It is obvious that $AlCl_3$ is not formed in the reaction.

Fraction No.	Boiling point	Yield (in %)	n_D^{20}	d_4^{20}
1	190—205°	20	1.5345	0.9993
2	205—210	20	1.5293	0.9982
3	210—215	26	1.5240	1.0040
4	215—220	8	1.5230	0.9968
5	220—225	16	1.5220	0.9915
6	225—230	11	1.5213	0.9872

• The isopropyl ether of phenol has the constants b.p. 176—177.2°, n_D^{20} 1.4992.

• • According to the literature data, o-isopropylphenol has the constants b.p. 214—214.5°, n_D^{20} 1.5315, d_4^0 1.012, m.p. of glycol ethers 130°.

SUMMARY

1. The alkylation of phenol with isopropyl chloride has been carried out. Gumbrin dried at 160—170° and activated by gaseous hydrogen chloride was used as the catalyst.

2. The isopropylphenol fractions were obtained in 56% yield, and from them were isolated o- and p-isopropylphenols.

LITERATURE CITED

[1] E. I. Barg, Technology of Synthetic Plastics. 407 (1954). *

[2] A. V Druzhinina, G. S. Tarmanyan, and I. V. Morozova, Chemistry and Technology of Fuels and Oils. 10, 41 (1957). *

[3] D. Frear, Chemistry of Insecticides and Fungicides. 69 (1948). * *

[4] A. Gurevich, Ber. 32, 2429 (1899).

[5] K. Andrianov, J. Gen. Chem. 6, 846 (1936).

[6] I. P. Tsukervanik and V. D. Tambovtseva, Bull. Central Asiatic Univ. 25, 221 (1937).

[7] I. F. Radzevenchuk, J. Gen. Chem. 28, 2423 (1958);* Auth. Cert. 116610 (1957).

[8] I. Niderl, S. Natelson, J. Am. Chem. Soc. 53, 1928 (1931).

[9] O. A. Reutov, Theoretical Problems of Organic Chemistry. 347 (1956). *

[10] K. A. Ogeloblin and T. V. Markina, J. Gen. Chem. 24, 1965 (1954). * * *

[11] A. K. Babko and I. V. Pyatnitskii, Quantitative Analysis. 217 (1956);* G. G. Gedroits, Selected Papers, II, 94 (1955). *

---

* In Russian.

* * Russian translation.

* * * Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF LIPIDES

I. SYNTHESIS OF TRIGLYCERIDES OF VEGETABLE OILS

I. K. Sarycheva, O. V. Utkina, M. E. Maurit, G. A. Vorob'eva

M. N. Bargaftik, N. A. Krit, A. I. Sherle, and N. A. Preobrazhenskii

Moscow Institute of Fine-Chemical Technology

Contemporary physicochemical methods of investigating fats and oils (chromatography, countercurrent distribution, and spectrophotometry) [1] permit only a conjectural judgment concerning their glyceride composition since they make it possible to determine not the individual compounds, but mixtures of components with a certain number of double bonds but of different structure and relative distribution of the acid substituents. In isolated cases more exact results can be obtained by a study (of freezing point curves, infrared spectra, and x-ray analysis data) of natural oils and comparison with the corresponding properties of a mixture of synthetic glycerides [2].

It have been established by investigations in recent years [3] that there are glycerides with a total of 4 to 9 double bonds in the composition of a number of vegetable oils. The different distribution and combination of the acid radicals in the molecules of the triglycerides makes possible the existence of a large number of isomers. (For example, for the triglycerides of linseed oil, which contain oleic, linoleic, linolenic, and stearic acid groups, the existence of 27 isomers is possible). The synthesis of these triglycerides and the study of their physicochemical properties, and also of the properties of mixtures of them is of great significance to the solution of the problem of the synthetic preparation of vegetable oils.

The synthesis of the simple (R'=R"=R''') and the mixed (R'=R"≠R''' and R'≠R"≠R''') triglycerides (XV) most frequently starts with the acid chlorides (VI) and glycerol (I), one (α) or two (α and α', α and β) hydroxyl groups of which are first protected with the aid of acetone [4] (II), triphenylchloromethane [5] (III and IV), benzaldehyde [6] (V), and other materials [7].

The substituted monoglycerides (VII, VIII, IX) or the corresponding diglyceride (X) obtained, depending on the reagents used [5, 8], are converted either to the α-(XI) and β-(XII)-monoglycerides, or to the α, α'-(XIII) and α, β-(XIV)-diglycerides, which then are acylated with the acid chlorides (VI).

In the present article are described the synthesis and the principal physicochemical properties of α-stearyl-β, α'-dilinolenin (SLnLn), α-stearyl-β-linolenyl-α'-linolein (SLnL), α-linoleyl-β, α'-dilinolenin (LLnLn), trilinolein (LLL), α, α'-dilinoleyl-β-linolenin (LLnL), and α, α'-dilinolenyl-β-stearin (LnSLn).*

The synthesis of these compounds was based on the reaction of the acid chlorides of stearic, linoleic, and linolenic acids with glycerol (I) and was carried out through a stage of the preparation of the monoglycerides: α-stearin, α-linolein, and α-linolenin (diagram, route a). Conversion of the monosubstituted glycerol derivatives to the triglycerides was accomplished either in one stage (for the synthesis of SLnLn, LLnLn, and LLL) or in two steps (for SLnL, LLnL, and LnSLn) through the diglycerides: α-stearyl-α'-linolein, α, α'-dilinolein, and α, α'-dilinolenin, without protection of the α'-hydroxyl group of the starting α-monoglycerides.

Thus, by maintaining a certain order in the creation of the ester groupings in the starting molecule of glycerol and by taking into account the different reactivity of the α' and β-hydroxyl groups of the monoglycerides,

---

*The letters designate acid radicals: S = stearic, O = oleic, L = linoleic, and Ln = linolenic.

$(CH_3)_2CO$ a   2CH₂OH   b C_6H_5CHO

βCHOH

2'CH₂OH

(I) $(C_6H_5)_3CCl$

CH₂OH
CHO   C(CH₃)₂
CH₂O
(II)

CH₂OC(C₆H₅)₃
CHOH
CH₂OH
(III)

CH₂OC(C₆H₅)₃
CHOH
CH₂OC(C₆H₅)₃
(IV)

CH₂O
CHOH CHC₆H₅
CH₂O
(V)

RCOCl (VI)   (VI)   (VI)   (VI)

CH₂OOCR
CHO   C(CH₃)₂
CH₂O
(VII)

CH₂OC(C₆H₅)₃
CHOOCR
CH₂OOCR
(X)

CH₂OC(C₆H₅)₃
CHOOCR
CH₂OC(C₆H₅)₃
(VIII)

CH₂O
CHOOCR·CHC₆H₅
CH₂O
(IX)

CH₂OOCR'
CHOH
CH₂OH
(XI)

CH₂OOCR'
CHOH
CH₂OOCR'''
(XIII)

CH₂OH
CHOOCR''
CH₂OOCR'''
(XIV)

(XI)

CH₂OH
CHOOCR''
CH₂OH
(XII)

(XI)

CH₂OOCR'
CHOOCR''
CH₂OOCR'''
(XV)

we prepared a series of triglycerides that were supposed components of a number of vegetable oils of symmetrical and unsymmetrical structure with a total of 5 to 8 double bonds.

TABLE 1

Physicochemical Constants of Triglycerides

Compound	n_D^{30}	d_4^{30}	Iodine No.
SLnLn	1.4820	0.9336	171.7
SLnL	1.4761	0.9335	136.6
LLnLn	1.4832	0.9318	231.3
LLL	1.4793	0.9272	171.5
LLnL	1.4840	0.9334	201.8
LnSLn	1.4819	0.9417	174.0

Through the example of the investigation of the properties of the compounds that were synthesized it can be seen that in going from the monoglycerides to the diglycerides SL, LL, LnLn and to the triglycerides SLnLn, SLnL, LLnLn, LLL, LLnL, LnSLn there is a gradual decrease in the specific gravity. It also is interesting to note that the physicochemical constants found for the triglycerides prepared (iodine number, d_4^{20}, n_D^{20}) are close to those for the natural vegetable oils (Tables 1 and 2).

EXPERIMENTAL

1. α-Stearyl-β, α'-dilinolenin (XV, R' = $C_{17}H_{35}$, R" = R"' = $C_{17}H_{29}$). To a mixture of 3.38 g of α-mono-stearylglycerol (XI, R' = $C_{17}H_{35}$) (m.p. 80.5−81 5°) and 3.0 g of quinoline at 0° was added, over the course of 30 minutes, a solution of 7.0 g of linolenic acid chloride (VI, R = $C_{17}H_{29}$) (b.p. 151−152° at 0.4 mm, d_4^{20} 0.9372, n_D^{20} 1.4812; MR$_D$ 90.19. $C_{18}H_{29}OCl$ F₃. Calculated 89.17. I no. 254.1; calc. 256.5). The reaction mixture was

TABLE 2

Physicochemical Constants of Vegetable Oils [9]

Vegetable oil	n_D^t	d_t^t	Iodine No.
Poppy seed	1.473—1.475 (25°)	0.921—0.937 (20°)	128—157
Linseed	1.480—1.485 (20°)	0.931—0.938 (15°)	170—205
Cameline seed	1.470 (20°)	0.920—0.930 (20°)	133—155
Soybean	1.472—1.4751(25°)	0.921—0.931 (20°)	186—195

heated in a current of nitrogen to boiling for 5 hours, then cooled to 5—6°, 250 ml of ether was added, and the mixture was acidified with 12 ml of 10% sulfuric acid. The upper layer was separated off, then washed consecutively with 150 ml of water, 20 ml of 10% potassium carbonate solution, and 100 ml of saturated aqueous sodium chloride solution, and dried with sodium sulfate. The solvent was distilled off in vacuo (15 mm). The residue (6.2 g) was washed with 70 ml of alcohol at 18° and 45 ml at 60°, after which it was dissolved in 50 ml of dry acetone, passed through a layer of activated carbon (20 × 50 mm), cooled to —65°, and left to stand under these conditions for 30—35 minutes. The mother liquor was separated from the precipitate, which was recrystallized from 25 ml of acetone with gradual cooling. The material that crystallized at —18° was filtered from the liquid phase. The mother liquor was cooled to —45°. To the precipitate obtained in this way after distilling off the acetone was added 30 ml of dry ether, the solution was passed through a chromatographic column with aluminum oxide (20 × 100 mm), eluted with 150 ml of ether, and the solvent was removed. Yield 1.1 g (9.6%).

M.p. -1—0°, d_4^{20} 0.9336, n_D^{20} 1.4820, MR_D 268.7; Calc. 267.59

Found %: C 77.60, 77.7; H 11.24, 11.22. I no. 171.7. $C_{57}H_{98}O_6F_6$ Calculated %: C 77.83; H 11.23. I no. 173.2.

2. α-Stearyl-β-linolenyl-α'-linolein (XV, R' - $C_{17}H_{35}$, R'' - $C_{17}H_{29}$, R''' = $C_{17}H_{31}$). To a solution of 14.0 g of α-stearyl-α'-linoleylglycerol (XIII, R' = $C_{17}H_{35}$, R''' = $C_{17}H_{31}$) (m.p. 35-36°, I. no. 81.08; calc. 81.74)prepared from α-monostearylglycerol (XI, R' = $C_{19}H_{35}$) and linoleic acid chloride (VI, R = $C_{17}H_{31}$) was added 10 g of linolenic acid chloride (VI, R = $C_{17}H_{29}$). The reaction mixture was heated in a current of nitrogen to boiling for 4 hours, then cooled to 18°, 80 ml of ether was added, the mixture was carefully stirred with 85 ml of 2.5% sulfuric acid, neutralized with saturated aqueous sodium bicarbonate solution, and dried with sodium sulfate. The residue after removal of the solvent was washed with boiling methanol (3 times with 30 ml portions) and subjected to fractional crystallization from acetone (1:5).

1st fraction 4.8 g, m.p. —(15—10°); 2nd fraction 2.4 g, m.p. —(25—20°), I no. 133.5; 3rd fraction 1.5 g (7.6%), m.p.-(45—40°), I no. 142.6, calc. 144.0; d_4^{20} 0.9335, n_D^{20} 1.4761, MR_D 266.40. $C_{57}H_{100}O_6F_8$. Calculated 268.05.

3. α-Linoleyl-β-, α'-dilinolenin (XV, R' = $C_{17}H_{31}$, R'' = R''' = $C_{17}H_{29}$). The synthesis was carried out under the conditions used for the preparation of α-stearyl-β, α'-dilinolenin from 3.4 g of α-monolinoleylglycerol (XI, R' = $C_{17}H_{31}$) (m.p. 13.5—15°, d_4^{20} 0.9741, n_D^{20} 1.4795, MR_D 103.3. $C_{21}H_{38}O_4F_2$. Calculated 102.95. I no. 142.9; calc. 143.2), 3.0 g of quinoline, and 7.0 g of linolenic acid chloride (VI, R = $C_{17}H_{29}$) in 40 ml of chloroform. In order to purify the material it was washed with 50 ml of alcohol at 18° and 30 ml at 60°, and then dissolved in 50 ml of ether and passed twice through a chromatographic column with aluminum oxide (10 × 100 mm) and a layer of activated carbon (2 g). Yield 1.5 g (18%).

Melting point of polymorphic forms —(53—52°) and —(17—16°), d_4^{20} 0.9318, n_D^{20} 1.4832, MR_D 268.4; calc. 266.649.

Found %: C 78.28, 78.30; H 11.03, 11.15. I no. 231.3. $C_{57}H_{94}O_6F_8$. Calculated %: C 78.21; H 10.82. I no. 232.1.

4. Trilinolein (XV, R' = R'' = R''' = $C_{17}H_{31}$). This compound was prepared similarly to α-linoleyl-β, α-dilinolenin from 13.5 g of α-monolinoleylglycerol (XI, R' = $C_{17}H_{31}$), 10.9 g of quinoline, and 23 g of linoleic acid chloride (VI, R' = $C_{17}H_{31}$) in 50 ml of chloroform; after 3 crystallizations from acetone (1:5) at —60°, 25 g (75%) was obtained.

M.p. $-(44-43°)$, d_4^{20} 0.9272, n_D^{20} 1.4793, MR_D 269.0; calc. 267.59.

Found %: C 78.16, 78.01; H 11.30, 11.28. I no. 171.5. $C_{57}H_{98}O_6F_6$. Calculated %: C 77.83; H 11.23. I no. 173.2.

5. α, α'-Dilinoleyl-β-linolenin (XV, R' = R''' = $C_{17}H_{31}$, R'' = $C_{17}H_{29}$). By the method used for the synthesis of α-stearyl-β-linolenyl-α'-linolein (XV, R' = $C_{17}H_{35}$, R'' = $C_{17}H_{29}$, R''' = $C_{17}H_{31}$), we obtained from 4.09 g of α, α'-dilinolein (XIII, R' = R''' = $C_{17}H_{31}$) (d_4^{20} 0.9602, n_D^{20} 1.4892. MR_D 185.08. $C_{39}H_{68}O_5F_4$. Calculated 185.27. I no. 164.3; calc. 165), prepared from α-monolinolein (XI, R' = $C_{17}H_{31}$), 2.38 g of linolenic acid chloride (VI, R' = $C_{17}H_{29}$), and 1.1 g of quinoline in 30 ml of chloroform, after recrystallization (from a mixture of 10 ml of methanol and 15 ml of acetone at $-60°$) and chromatographic purification (on a column filled with 40 g of aluminum oxide) 3.4 g (58.4%) of product.

d_4^{20} 0.9334, n_D^{20} 1.4840, MR_D 268.9; calc. 267.12.

Found %: C 77.95 78.01; H 11.10, 11.07. I no. 201.8. $C_{57}H_{96}O_6F_7$. Calculated %: C 78.02; H 11.02. I no. 202.5.

6. α, α'-Dilinolenyl-β-stearin (XV, R' = R''' = $C_{17}H_{29}$, R'' = $C_{17}H_{35}$). As in the preceding experiment, from α-monolinolenin (XI, R' = $C_{17}H_{29}$) (d_4^{20} 0.9834, n_D^{20} 1.4845, MR_D 102.60. $C_{21}H_{36}O_4F_3$. Calculated 102.47. I no. 218, calc. 216) and linolenic acid chloride (VI, R = $C_{17}H_{29}$) we obtained α, α'-dilinolenin (XIII, R' = R''' = $C_{17}H_{29}$) (d_4^{20} 0.9568, n_D^{20} 1.4839, MR_D 183.2 $C_{39}H_{64}O_5F_6$. Calculated 184.33. I no. 240; calc. 248.4). Then starting with 7.12 g of α, α'-dilinolenin, 3.8 g of stearic acid chloride (VI, R = $C_{17}H_{35}$) and 1.7 g of quinoline in 30 ml of chloroform, we obtained after purification from contaminants by washing (at 30° with five 25-ml portions of methanol and recrystallization (from 30 ml of ether at $-(8-5°)$ 2.47 g (24.2%) of product.

d_4^{20} 0.9401, n_D^{20} 1.4819, MR_D 266.62; calc. 267.59.

Found %: C 77.52, 77.67; H 11.29, 11.03. I no. 174.0. $C_{57}H_{96}O_6F_6$. Calculated %: C 77.83; H 11.23. I no. 173.2.

SUMMARY

1. The synthesis of α-stearyl-β, α'-dilinolenin (SLnLn), α-stearyl-β-linolenyl-α'-linolein (SLnL), α-linoleyl-β, α'-dilinolenin (LLnLn), trilinolein (LLL), α, α'-dilinoleyl-β-linolenin (LLnL), and α, α'-dilinolenyl-β-stearin (LnSLn), glyceride components of a number of vegetable oils, has been accomplished.

2. In the course of the synthesis. the following monoglycerides were isolated and characterized by their physicochemical constants: α-linoleyl- and α-linolenylglycerides; also the following diglycerides: α-stearyl-α'-linoleyl-α,α'-dilinoleyl-, and α, α'-dilinolenylglycerine.

LITERATURE CITED

[1] P. Quilin, H. J. Weiser Jr., J. Am. Oil. Chem. Soc. 35, 325 (1958); H. Schlenk, J. L. Gellerman, J. A. Tillotson, H. K. Mangold, J. Am. Oil. Chem. Soc. 34, 377 (1957); E. H. Ahlers, L. C. Craig, J. Biol. Chem. 195, 299 (1952); H. J. Dutton, J. Am. Oil. Chem. Soc. 32, 552 (1955); J. A. Monick, R. E. Treybal, J. Am. Oil. Chem. Soc. 33, 193 (1956); H. E. Ahlers, R. A. Breff, N. G. McTaggart, J. Appl. Chem. 3, 433 (1953).

[2] D. Chapman, A. C. Davies, J. Chem. Soc. 1957, 1502.

[3] F. T. Walker, M. R. Mills, J. Soc. Chem. Ind. 61, 125 (1952); F. T. Walker, M. R. Mills, J. Soc. Chem. Ind. 62, 106 (1943); F. T. Walker, M. R. Mills, J. Oil. Colour. Chem. Assoc. 28, 119 (1945); H. J. Dutton, J. A. Cannon, J. Am. Oil. Chem. Soc. 33, 46 (1956).

[4] B. F. Daubert, E. S. Lutton, J. Am. Chem. Soc. 69, 1447 (1947).

[5] E. Fischer, M. Bergman, H. Bärwind, Ber. 53, 1589 (1920).

[6] P. E. Verkade, Rec. trav. chim. 54, 716 (1935).

[7] F. J. Baur, J. Am. Chem. Soc. 73, 3926 (1951).

[8] J. B. Martin, J. Am. Chem. Soc. 75, 5482 (1953).

[9] L. P. Bezzubov, Chemistry of Fats. [In Russian] (Pischepromizdat, 1956) p. 220.

FROM THE FIELD OF ORGANIC INSECTOFUNGICIDES.

XLVIII. SYNTHESIS OF SOME AROMATIC ESTERS OF HALOPHENOXYACETIC ACIDS

N. N. Mel'nikov and I. L. Vladimirova

Scientific Institute for Fertilizers and Insectofungicides

In recent years it has been established that the halophenoxyacetic acids and their salts are not only herbicides, but also fungicides [1]. Some arylacetylhydroxyamines also have considerable fungicidal activity [2].

As is well known, going from the acids and the salts with inorganic and organic bases to the esters of the halophenoxyacetic acids substantially increases their physiological activity with respect to the higher plants [1]. Considering that metabolism in the lower plants has some similarity to metabolism in the higher ones, we might expect an increase in the fungicidal and fungistatic action on going from the acids and salts of the halophenoxyacetic acids to their esters in this case also.

Of especial interest was the study of the fungicidal action of the aromatic esters of 2, 4-dichlorophenoxy- and 2,4,5-trichlorophenoxyacetic acids, which are extremely active and readily available herbicides. In connection with these facts, we synthesized a number of esters of 2,4-dichlorophenoxy- 2,4,5-trichlorophenoxy-, and pentachlorophenoxyacetic acids with various phenols. The esters are not described in the literature. The synthesis of the esters was accomplished by reacting the appropriate acid chlorides with the alkali phenolates in aqueous medium. The compounds prepared by us and their properties are given in the table   Of the compounds studied, the most active fungicide was the pentachlorophenyl ester of 2,4,5-trichlorophenoxyacetic acid, which approached the organic mercury compounds in effect on fungi. The other esters were comparatively low in activity.

EXPERIMENTAL

The preparation of the esters of the halophenoxyacetic acids was carried out under the following conditions: In a flask with a reflux condenser, dropping funnel, and mechanical stirrer was placed 0.05 mole of halophenoxyacetic acid chloride (prepared from the acid and thionyl chloride), and an aqueous solution of 0.05 mole of the appropriate phenolate was added from the dropping funnel with good stirring. Then the reaction mixture was stirred for 2 hours at room temperature or 30 minutes while heating on a boiling water bath. After cooling, the precipitate was filtered off and recrystallized from an appropriate solvent. Most of the compounds were recrystallized 2—3 times until the melting point was constant. The compounds prepared and their properties are given in the table.

SUMMARY

1. By the reaction of halophenoxyacetyl chlorides with alkali phenolates a number of esters of 2,4-dichlorophenoxy- 2,4,5-trichlorophenoxy-, and pentachlorophenoxyacetic acids not described in the literature have been prepared.

2. A study of the fungicidal properties of the compounds synthesized has shown that almost all the esters have moderate activity. An exception is the pentachlorophenyl ester of 2,4,5-trichlorophenoxyacetic acid, which approaches the organic mercury compounds in fungicidal activity.

Properties of Esters of Halophenoxyacetic Acids

Formula	Melting point	Yield (in%)	% Cl	
			found	calculated
P-(CH$_3$)$_2$CHC$_6$H$_4$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4	103°	70	21.46, 21.60	20.90
P-O$_2$NC$_6$H$_4$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4	152	85	21.59, 21.55	21.75
o-HOCOC$_6$H$_4$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4	148—151	63	20.35, 20.08	20.82
2-HOOC–C$_6$H$_3$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4, 4-Br	143—145	38	42.56(C); 2.87 (H)	42.80 (C); 2.14 (H)
1-C$_{10}$H$_7$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4	156	71	20.86	20.42
2-C$_{10}$H$_7$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4	130—133	89	20.01, 20.40	20.42
1-CH$_3$C$_{10}$H$_6$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4	147—148	94	20.20	19.63
2-C$_6$H$_5$C$_6$H$_4$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4	96—97	98	18.20	18.90
2-C$_6$H$_5$–C$_6$H$_3$OCOCH$_2$OC$_6$H$_3$Cl$_2$-2,4, 4-Cl	140	98	25.70, 25.78	26.07
P-(CH$_3$)$_2$CHC$_6$H$_4$OCOCH$_2$OC$_6$H$_2$Cl$_3$-2,4,5	211—213	75	29.00, 28.81	28.46
2-HOOC–C$_6$H$_3$OCOCH$_2$OC$_6$H$_2$Cl$_3$-2,4,5, 4,6-Cl$_2$	149—150	63	40.68	40.20
1-C$_{10}$H$_7$OCOCH$_2$OC$_6$H$_2$Cl$_3$-2,4,5	142	76	28.40, 28.44	27.81
C$_6$H$_5$OCOCH$_2$OC$_6$Cl$_5$	276—278	85	44.78, 44.26	44.76
C$_6$Cl$_5$OCOCH$_2$OC$_6$H$_2$Cl$_3$-2,4,5*	169—170	82	55.92, 56.93	56.31

*In the literature only the testing of this compound as a herbicide has been described [3]; the manner of preparing it and its properties are not indicated.

LITERATURE CITED

[1] N. N. Mel'nikov, Yu. A. Baskakov, and K. S. Bokarev, Chemistry of the Herbicides and Plant Growth Stimulators.* (Goskhimizdat, Moscow, 1954); P. L. Zakharchenko, N. N. Mel'nikov, A. A. Rusakova, A. V. Skalozubova, M. S. Chesnokova, and S. E. Raskin, Auth. Cert. No. 100070 (1955).

[2] Z. Ickstein, T. Urbanski, Przem. Chem. 12, 640 (1956).

[3] H. Thompson, C. Swanson, A. Norman, Botan. Gaz. 107, 476 (1946).

* In Russian.

FROM THE FIELD OF ORGANIC INSECTOFUNGICIDES

XLIX. THE CONDENSATION OF SOME UNSATURATED COMPOUNDS
WITH HEXACHLOROCYCLOPENTADIENE

N. A. Belikova, L. G. Vol'fson, K. V. Kuznetsova

N. N. Mel'nikov, and A. F. Platé

Scientific Institute for Fertilizers and Insectofungicides and Institute of

Organic Chemistry of the Academy of Sciences USSR.

In connection with a search for new effective insecticides in recent years much attention has been devoted to the study of the reaction of polyhalocyclopentadienes with various olefins and cycloolefins [1]. As a result of these investigations there have been found not only a number of effective insecticides, but also substances useful for the production of high-molecular compounds [2].

In the development of our earlier investigations in the study of the reaction of polyhalocyclopentadienes with various olefins [3], we undertook a study of the reaction of hexachlorocyclopentadiene with cyclic unsaturated compounds containing short chains in the ring. In the present communication we describe the condensation of hexachlorocyclopentadiene with:1-vinylcyclohexene-3; tetrahydroindene; 2-vinylbicyclo- (2,2,1)-heptene-5; 2-vinyl-1,4-endomethylene-1,2,3,4,5,5a,8,8a-octahydronaphthalene; and 1,4,5,8-diendomethylene-1,4,4a,5,8,8a-hexahydronaphthalene. The reaction proceeds when the reactants are heated to 100—130°.

When hexachlorocyclopentadiene is reacted with 1-vinylcyclohexene-3, the formation of two isomeric products (I) and (II) is possible. However, it is more probable that compound (I) will be obtained, since the double bond of the vinyl group is more reactive than the double bond in the cyclohexane ring. This is confirmed by numerous examples of similar processes. It is possible that in our case a mixture of the two isomers is obtained, with (I) predominating. A mixture of the two isomers is obtained, apparently, also when hexachlorocyclopentadiene is reacted with 2-vinylbicyclo-(2, 2, 1)-heptene-5. When two molecules of hexachlorocyclopentadiene react with a molecule of 2-vinylbicyclo-(2, 2, 1)-heptene-5, a compound of structure (V) is formed.

Condensation of hexachlorocyclopentadiene with tetrahydroindene, 2-vinyl-1,4-endomethylene-1,2,3,4,5, 5a,8,8a-octahydronaphthalene, and (2,3-cyclopenteno)-1,4-endomethylene-1,2,3,4,5,5a,8,8a-octahydronaphthalene also in each case may yield a mixture of two products, which it has not thus far been possible to separate.

The structure of the compounds synthesized by us and their properties and also the constants of the starting hydrocarbons are given in Table 1. All the compounds synthesized proved to be practically nontoxic to insects.

EXPERIMENTAL

Starting materials. 1-Vinylcyclohexene was prepared by dimerization of butadiene. 2-Vinylbicyclo-(2,2,1)-heptene-5 and tetrahydroindene were prepared by the condensation of cyclopentadiene with butadiene, and diendomethylenehexahydronaphthalene by the condensation of bicyclo-(2,2,1)-heptadiene-2,5 with cyclopentadiene; it is a byproduct in the preparation of bicyclo- (2,2,1)-heptadiene-2,5 from acetylene and cyclopentadiene [4]. 2-Vinyl-1,4-endomethylene-1,2,3,4,5,5a,8,8a-octahydronaphthalene was synthesized from 2-vinylbicyclo-(2,2,1)-heptene-5 and butadiene, and (2,3-cyclopenteno)-1,4-endomethylene-1,2,3,4,5,5a,8,8a-octahydronaphthalene was synthesized from the dimer of cyclopentadiene and butadiene. Hexachlorocyclopentadiene had the following constants: b.p. 114—116° (16 mm), d_4^{20} 1.7101, n_D^{20} 1.5637.

Condensation Products of Hexachlorocyclopentadiene with Cyclic Unsaturated Hydrocarbons
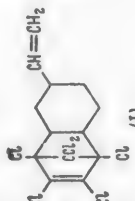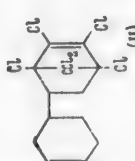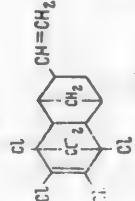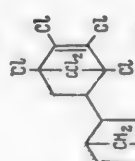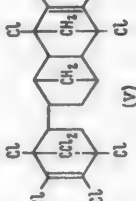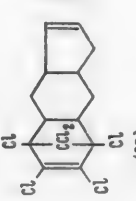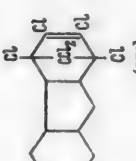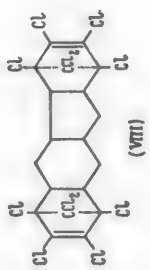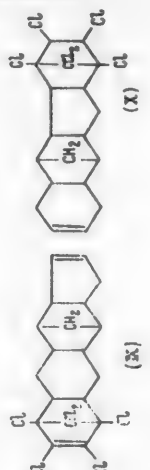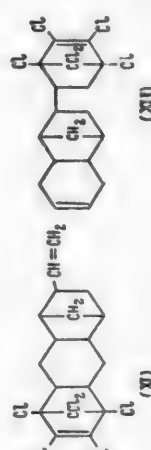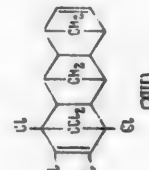
Formula	Yield (in %)	Temperature		d_4^{20}	n_D^{20}	MR_D		% Cl		Constants of starting hydrocarbons		
		melting	boiling (pressure in mm)			found	calc.	found	calc.	boiling point (pressure in mm)	d_4^{20}	n_D^{20}
	48	—	146—150° (0.25)	1.500	1.5671	82.97	83.89	55.57, 55.30	55.80	129—130° (760)	—	1.4652
	53	—	160—164 (0.25)	1.5190	1.5680	84.21	86.31	54 28, 53.91	54.19	140.3—140.4 (760)	0.8884	1.4805
	28	201—203°	—	—	—	—	—	63. 8, 63.25	63.96	140.3—140.4 (760)	0.8884	1.4805
	51	132—135	—	—	—	—	—	54.70, 55.21	54.19	160.3 (760)	0.9261	1.4980

TABLE 1 (continued)

Formula	Yield (in %)	Temperature melting	Temperature boiling (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	% Cl found	% Cl calc.	Constants of starting hydrocarbons boiling point (pressure in mm)	d_4^{20}	n_D^{20}
(VIII) (X)	25	250 (decomp.)	—	—	—	—	—	63.42, 64.42	63.96	160.3 (760)	0.9261	1.4980
(IX) (XII)	57	136—142	—	—	—	—	—	45.97, 45.50	46.40	m. p. 36°		
(XI)	54	—	166—172 (0.22)	1.5160	1.5755	97.62	90.12	47.15, 47.35	47.65	75.0—75.1 (1.5)	0.9639	1.5145
(XIII)	50	135—136	—	—	—	—	—	49.47, 49.40	49.36	217 (760)	1.0374	1.5322

<u>Condensation of hexachlorocyclopentadiene with unsaturated hydrocarbons</u>. Depending on the product prepared, 2 moles or 0.5 mole of hydrocarbon was used to 1 mole of hexachlorocyclopentadiene. The mixture of hydrocarbon and hexachlorocyclopentadiene was heated in sealed tubes at 110—130° for 30 hours. After cooling, the reaction mixture was fractionated in high vacuum and, for crystalline compounds, was recrystallized from an appropriate solvent (most frequently from methyl alcohol) and analyzed.

SUMMARY

In order to study their insecticidal properties, a number of compounds that have not been described in the literature were synthesized by the condensation of hexachlorocyclopentadiene with cyclic unsaturated hydrocarbons.

It has been shown that the condensation of hexachlorocyclopentadiene with cyclic hydrocarbons proceeds on prolonged heating of a mixture of the reactants at 120-150°.

The compounds prepared were not insecticidally active.

LITERATURE CITED

[1] N. N. Mel'nikov and L. G. Vol'fson, Chem. Indus. No. 10, 45 (1953); L. G. Vol'fson, Chem. Agents for Plant Protect. No. 2, 23 (1957); H. E. Ungnade, E. T. McBee, Chem. Revs. <u>58</u>, 249 (1958); P. Müller, M. Spindler, Exper. <u>10</u>, 115 (1954); R. L. Metcalf. Organic Insecticides. (New York, 1955).

[2] P. Robitschec, C. Bean, Ind. Eng. Ch. <u>46</u>, 1628 (1954).

[3] L. G. Vol'fson, N. N. Mel'nikov, A. F. Platé, Yu. N. Sapozhkov, and G. S. Taits, Proc. Acad. Sci. USSR <u>105</u>, 1252 (1955); Proc. NIUIF <u>158</u>, 235 (1958); S. S. Kukalenko and N. N. Mel'nikov, J. Gen. Chem. <u>28</u>, 157 (1958);* S. S. Kukalenko, N. N. Mel'nikov, T. I. Naryshkina, and N. I. Shuikin, J. Gen. Chem. 28, 480 (1958);* S. D. Volodkovich, N. N. Mel'nikov, A. F. Platé, and M. A. Pryanishnikova, J. Gen. Chem. 28, 3123 (1958);* N. N. Mel'nikov and S. D. Volodkovich, J. Gen. Chem. 29, 3317 (1959).*

[4] A. F. Platé and M. A. Pryanishnikova, Bull. Acad. Sci. USSR, Div. Chem. Sci. 741 (1956).*

FROM THE FIELD OF ORGANIC INSECTOFUNGICIDES

L. SYNTHESIS OF SOME MIXED ESTERS OF DITHIOPHOSPHORIC ACID

K. D. Shvetsova-Shilovskaya, N. N. Mel'nikov, and V. A. Glushenkov

Scientific Institute for Fertilizers and Insectofungicides

In connection with a search for new active insecticides, in recent years a large number of extremely varied mixed esters of dithiophosphoric acid have been synthesized and described, some of which have received practical use in agriculture. However, among the large number of derivatives of dithiophosphoric acid that have been studied, compounds containing two dithiophosphoric acid groups in the molecule have been almost absent. The only exception is methylene bis (diethyldithiophosphate), which very recently has been proposed for use as an insecticide and acaricide. •

In connection with these facts, we undertook the synthesis of some compounds of this type, and first in order was the synthesis of alkylene bis (dialkyldithiophosphates) with the general formula $(ROPSS)\,2(CH_2)_n$, where $n = 1-4$, by the reaction of salts of the dialkyldithiophosphoric acid with the appropriate halogen derivatives of hydrocarbons. The compounds prepared by us and their properties are given in the table; of them only methylene bis-(diethyldithiophosphate) has been described in the literature, and for it even the most important constants are lacking.

A study of the insecticidal properties of the compounds synthesized by us carried out by P. V. Popov and N. S. Ukrainets showed that most of them were weakly active.

EXPERIMENTAL

The preparation of the alkylene bis (dialkyldithiophosphates) was carried out under the following conditions: In a flask with a reflux condenser and mechanical stirrer was placed a mixture of the dihalogen derivative and potassium dialkyldithiophosphate and alcohol. The reaction was carried out in the medium of the alcohol, the radical of which entered into the composition of the potassium dialkyldithiophosphate (this method was employed to avoid transesterification of the dialkyldithiophosphates). The mixture obtained was boiled for 2—4 hours with good stirring. The potassium halide that precipitated was filtered off and the filtrate was treated with water. The water layer was extracted with benzene, dried over calcium chloride, and the solvent was distilled off in vacuo. The material obtained was fractionated in high vacuum and analyzed. Some of the materials that did not distil without decomposition were analyzed without distillation. However, light fractions were distilled off from them in high vacuum on a boiling water bath.

The compounds prepared by us and their properties are given in the table.

SUMMARY

By the reaction of dihaloalkanes with salts of dialkyldithiophosphoric acids, a number of alkylene bis (dialkyldithiophosphates) that have not been described in the literature were synthesized. All the compounds prepared were comparatively weak insecticides.

•Agric. Chem. 13, 32 (1958).

Properties of Mixed Esters of Dithiophosphoric Acid

Formula	Yield (in%)	Boiling point (pressure in mm)	d_4^{20}	n_g^{20}	% P found	% P calc.
$[(C_2H_5O)_2PSS]_2CH_2$	35	164—165° (0.3)	1.2277	1.5478	15.75	16.11
$[(C_3H_7O)_2PSS]_2CH_2$	49	175—176 (0.1)	1.1630	1.5276	14.02, 14.14	14.06
$[(iso\text{-}C_3H_7O)_2PSS]_2CH_2$	58	—	1.1539	1.5258	14.20, 14.15	14.06
$[(C_4H_9O)_2PSS]_2CH_2$	45	—	1.1084	1.5153	12.46, 12.48	12.47
$[(iso\text{-}C_4H_9O)_2PSS]_2CH_2$	41	—	1.0919	1.5103	12.65, 12.60	12.47
$[(C_2H_5O)_2PSS]_2(CH_2)_2$	35	187 (0.25)	1.2188	1.5427	15.42, 15.68	15.54
$[(C_3H_7O)_2PSS]_2(CH_2)_2$	34	185—186 (0.2)	1.1638	1.5265	13.45, 13.62	13.28
$[(iso\text{-}C_3H_7O)_2PSS]_2(CH_2)_2$	72	—	1.1790	1.5268	13.37, 13.68	13.62
$[(C_4H_9O)_2PSS]_2(CH_2)_2$	73	—	1.1045	1.5156	11.96, 11.78	12.13
$[(iso\text{-}C_4H_9O)_2PSS]_2(CH_2)_2$	28	—	1.1006	1.5143	12.22, 12.24	12.13
$[(C_2H_5O)_2PSS]_2(CH_2)_3$	69	192 (0.35)	1.1922	1.5402	15.22, 15.21	15.01
$[(C_2H_5O)_2PSS]_2(CH_2)_4$	59	204 (0.22)	1.1783	1.5335	14.57, 14.53	14.52

THE FULL ESTERS OF THE ISOMERIC CHLOROFLUOROETHANE PHOSPHONIC ACIDS

Yu. M. Zinov'ev, T. G. Spiridonova and L. Z. Soborovskii

It has been shown previously that treatment of vinyl chloride or fluoride with phosphorus trichloride under oxidizing conditions gives the isomeric acid chlorices of the corresponding ethane phosphonic acids [1,2]:

$$CH_2=CHCl + 2PCl_3 + O_2 \longrightarrow \begin{cases} CH_2ClCHClP(O)Cl_2 \\ CHCl_2CH_2P(O)Cl_2 \end{cases} + POCl_3$$
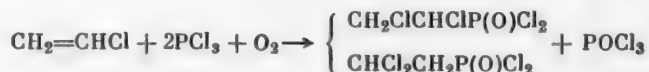
In this paper we describe the synthesis and properties of the esters obtained from the isomeric acid chlorides of chlorofluoroethane phosphonic acid, $C_2H_3FClP(O)Cl_2$.

In order to establish their structures, the same esters were synthesized from the acid chloride obtained by the treatment of 1-chloro-2-fluoroethane with phosphorus trichloride under oxidizing conditions [3].

The following isomers could be obtained in this way.

A. From vinyl fluoride:

$$CH_2=CHF - \begin{cases} \rightarrow CH_2ClCHFP(O)Cl_2 & \quad (1) \\ \rightarrow CHFClCH_2P(O)Cl & \quad (2) \end{cases}$$

B. From 1-chloro-2-fluoroethane:

$$FCH_2CH_2Cl - \begin{cases} \rightarrow CH_2FCHClP(O)Cl_2 & \quad (3) \\ \rightarrow CH_2ClCHFP(O)Cl_2 & \quad (4) \end{cases}$$
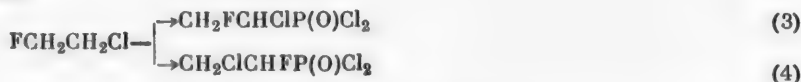
The structures of isomers (1) and (4) are identical. Each of the other two isomers, (2) and (3), can only be formed from one of the starting compounds: (2) from vinyl fluoride and (3) from 1-chloro-2-fluoroethane. The di-acid chloride obtained from vinyl fluoride (I) boiled at a somewhat higher temperature than that from 1-chloro-2-fluoroethane (II), and also differed from it in density. In neither case was it possible to separate isomers by fractionation.

Both acid chlorides (A and B) reacted with alcohols (methyl, ethyl, and isobutyl) to give two series of full esters of chlorofluoroethane phosphonic acid, $C_2H_3FClP(O)(OR)_2$. In all cases the esters obtained from vinyl fluoride (series A) boiled about 20° higher than those from chlorofluoroethane (Series B). The two series of compounds, A and B, also differed in their chemical behavior. The compounds of series A, on treatment with tri-ethylamine, relatively easily lost a molecule of hydrogen chloride to form dialkyl esters of 2-fluoroethene phosphonic acid, $CHF=CHP(O)(OR)_2$ (this reaction was shown, for instance by the diethyl ester of chlorofluoroethane phosphonic acid). The esters of series B split off hydrogen chloride very slowly and to a much less extent. It is thus clear that there was a structural difference between the substances of series A and B. The course of dehydrochlorination, for each of the six esters under consideration, is shown in the figure.

By analogy with the behavior of the esters, obtained from the acid chlorides formed by the treatment of vinyl chloride with phosphorus trichloride under oxidizing conditions, it may be presumed that dehydrochlorination

proceeds more readily with derivatives of 2,2-dihalogenoethane phosphonic acid [1]. It is therefore probable that the main bulk of the product of treating vinyl fluoride with phosphorus trichloride under oxidizing conditions corresponded to compound (2).

The esters of series B only lost very little hydrogen chloride on treatment with triethylamine. This loss was probably due to ester produced from the acid chloride of structure (3), since derivatives of (1), and consequently of (4), should be stable to such treatment. The esters were practically unhydrolyzed by water. An exception was the dimethyl ester of chlorofluoroethane phosphonic acid, synthesized from vinyl fluoride (III).

The table shows the fundamental constants and yields of the compounds synthesized.

Compound IX was obtained by the dehydrochlorination of V; X was the material left over from V which did react with triethylamine.

The esters obtained were tested as insecticides. Some of them showed physiological activity, so that precautions should be taken when working with them.

EXPERIMENTAL

1. Methyl esters of the isomeric chlorofluoroethane phosphonic acids.

a) The acid chloride of chlorofluoroethane phosphonic acid (I) (11.7 g, 0.058 mole), obtained by the treatment of vinyl fluoride with phosphorus trichloride under oxidizing conditions [2], was added drop by drop to 50 ml of methanol at −10°. The reaction mixture yielded 7.2 g of III.

Found %: Cl 19.40, 19.62; P 16.47, 16.01; OCH_3 31.97, 32.13.

b) Under the same conditions, 10.0 g (0.05 mole) of the acid chloride of chlorofluoroethane phosphonic acid (II) obtained by the treatment of 1-chloro-2-fluoro-ethane [3] with phosphorus trichloride under oxidizing conditions, yielded 7.4 g of IV.

Found %: Cl 15.81; P 15.57; OCH_3 32.67, 32.53. Calculated %: $C_4H_9O_3PClF$: Cl 18.61; P 16.25; OCH_3 32.56.

2. Ethyl esters of the isomeric chlorofluoroethane phosphonic acids.

a) Under the same conditions as 1, 15.5 g of V was obtained from 16.0 g (0.08 mole) of I and 50 ml of anhydrous alcohol.

Found %: P 14.10, 13.85; OC_2H_5 40.08, 40.41.

b) Under the same conditions as 1, 12.0 g of VI was obtained from 12.3 g (0.061 mole) of II and 50 ml of anhydrous alcohol.

Found %: P 14.01, 13.78; OC_2H_5 43.03, 42.90. Calculated %: $C_6H_{13}O_3PClF$: P 14.17; OC_2H_5 41.22.

3. Isobutyl esters of the isomeric chlorofluoroethane phosphonic acids.

a) Under the same conditions as 1, 2.5 g of VII was obtained from 3.8 g (0.019 mole) of I and 17 ml of isobutyl alcohol.

Found %: C 43.58, 43.80; H 6.00, 6.24; P 11.46, 11.59.

b) Under the same conditions as 1, 23.3 g of VIII was obtained from 25.0 g (0.125 mole of II and 60 ml of isobutyl alcohol.

Found %: C 42.69, 43.03; H 7.56, 8.02; P 10.87, 10.90. Calculated %: $C_{10}H_{21}O_3PClF$: C 43.72; H 7.10; P 11.27.
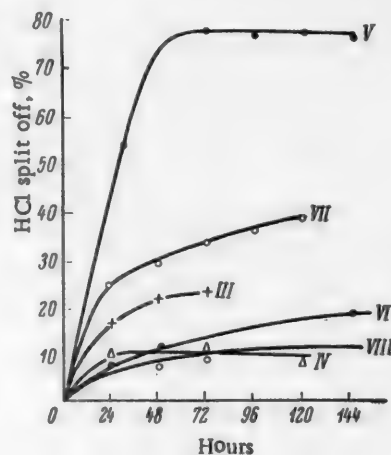
Compd	Formula	Series	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR found	MR calculated	Yield, %
(I)	C₂H₃FClP(O)Cl₂ *	A	108—110° (30)	1.6531	1.4715	33.78	34.33	6
(II)	C₂H₃FClP(O)Cl₂ **	B	98—100 (30)	1.6279	1.4600	33.55	34.33	12
(III)	C₂H₃FClP(O)(OCH₃)₂	A	97 (3)	1.3730	1.4275	36.19	36.86	65
(IV)	C₂H₃FClP(O)(OCH₃)₂	B	74—77 (1)	1.3750	1.4170	34.83	35.86	78
(V)	C₂H₃FClP(O)(OC₂H₅)₂	A	115—116 (3)	1.2425	1.4270	45.13	45.61	88
(VI)	C₂H₃FClP(O)(OC₂H₅)₂	B	93—95 (2)	1.2506	1.4214	44.38	45.61	89
(VII)	C₂H₃FClP(O)(OC₄H₉-iso)₂	A	143—145 (2.5)	1.1300	1.4381	62.85	62.43	48
(VIII)	C₂H₃FClP(O)(OC₄H₉-iso)₂	B	135—136 (3)	1.1157	1.4231	64.03	62.43	68
(IX)	CHF=CHP(O)(OC₂H₅)₂	A	76—77 (3.5)	1.1706	1.4140	38.86	40.28	—
(X)	CH₂ClCHFP(O)(OC₂H₅)₂	A	118—121 (5)	1.2444	1.4270	45.11	45.61	—

* Described previously [2].

** Described previously [3].

4. Diethyl esters of 2-fluoroethene phosphonic acid (IX) and of 2-chloro-1-fluoroethane phosphonic acid (X). The mixed isomers V (10.0 g = 0.045 mole) were treated with 4.6 g (0.045 mole) of triethylamine; the triethylamine hydrochloride formed was filtered off the next day, and the filtrate was fractionated under reduced pressure. The yield of IX was 1.1 g.

Found %: OC₂H₅ 48.65, 48.47. Calculated %: C₆H₁₂O₃PF: OC₂H₅ 49.48.

The yield of X (the higher boiling fraction) was 4.8 g.

Found %: OC₂H₅ 40.5, 39.85. Calculated %: C₆H₁₃O₃PClF: OC₂H₅ 41.22.

5. Dehydrochlorination of the dialkyl esters of chlorofluoroethane phosphonic acid with triethylamine. A sample of the ester was mixed with an equal weight of triethylamine, and maintained at 20° for a definite time (1 to 7 days); the mixture was then treated with water, and the chloride ion content was determined in the resulting solution. The analytical results are shown in the figure.

SUMMARY

1. The treatment of vinyl fluoride with phosphorus trichloride under oxidizing conditions yields two isomeric products—the acid chlorides of 1-chloro-2-fluoro- and 2,2-chlorofluoro-ethane phosphonic acids.

2. The treatment of 1-chloro-2-fluoroethane with phosphorus trichloride under oxidizing conditions yields a mixture of the isomeric acid chlorides of 2-chloro-1-fluoro- and 1-chloro-2-fluoro-ethane phosphonic acids.

3. The methyl, ethyl, and isobutyl esters of the isomeric chlorofluoroethane phosphonic acids and the ethyl esters of 2-fluoroethene and 2-chloro-1-fluoroethane phosphonic acids have been synthesized.

4. The dehydrochlorination of these synthesized alkyl esters of chlorofluoroethane phosphonic acids with triethylamine has been investigated.

LITERATURE CITED

[1] L. Z. Soborovskii, Yu. M. Zinov'ev, and L. I. Muler, Doklady Akad. Nauk SSSR 109, 98 (1956). *

[2] L. Z. Soborovskii, Yu. M. Zinov'ev, and T. G. Spiridonova, Zhur. Obschei Khim. 29, 1139 (1959). *

[3] Yu. M. Zinov'ev and L. Z. Soborovskii, Zhur. Obschei Khim. 29, 2645 (1959). *

* Original Russian pagination. See C. B. Translation.

THE REACTIONS OF CHLOROALKYLALKYLALKYLALKOXYSILANES WITH POLYHYDRIC ALCOHOLS.

K. A. Andrianov and M. A. Golubenko

The V. I. Lenin All-Union Electrotechnical Institute

The reactions of polyhydric alcohols with alkylalkoxysilanes, used for the synthesis of ethers [1], have been described in the literature. It was of interest to investigate whether this etherification exchange reaction could be applied to halogenoalkylalkylalkoxysilanes. Since the exchange etherification of the alkoxyl groups in alkylalkoxysilanes with polyhydric alcohols takes place at elevated temperatures $(110-140°)$ [2], it might be anticipated that the reaction of alcohols with chloroalkylalkoxysilanes would be accompanied by a side reaction, because of the mobility of the halogen of a chloromethyl group and of the susceptibility of the CH_2Cl and $CHCl_2$ groups to splitting off.

The exchange etherification of chloroalkylalkylalkoxysilanes with polyhydric alcohols was investigated, using as examples the reactions of ethylene glycol, glycerine and hydroquinone with chloromethyldimethylethoxysilane and dichloromethyldimethylethoxysilane.

The reactions of ethylene glycol with chloromethyldimethylethoxysilane and dichloromethyldimethylethoxysilane took place with the formation of the bis (chloromethyldimethylsilyl) and bis (dichloromethyldimethylsilyl) diethers of ethylene glycol.

$$2R(CH_3)_2SiOC_2H_5 + HOCH_2CH_2OH \longrightarrow$$
$$\longrightarrow R(CH_3)_2SiOCH_2CH_2OSi(CH_3)_2R + 2C_2H_5OH$$
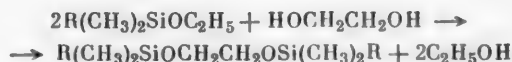
where R is CH_2Cl or $CHCl_2$.

The yield was 80%. The structures of the products were established by analysis and by their hydrolysis in weakly acid media to bis (chloromethyl)-tetramethyldisiloxane or bis (dichloromethyl) tetramethyldisiloxane and ethylene glycol, in accordance with the reaction:

$$R(CH_3)_2SiOCH_2CH_2OSi(CH_3)_2R + H_2O \longrightarrow R(CH_3)_2SiOSi(CH_3)_2R +$$
$$+ HOCH_2CH_2OH,$$
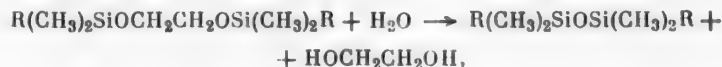
where R is CH_2Cl or $CHCl_2$.

Glycerine reacted with chloromethyldimethylethoxysilane and dichloromethyldimethylethoxysilane to form the exchange ethers in 73% yield, in accordance with the reaction:

$$\begin{array}{c} 3R(CH_3)_2SiOC_2H_5 \\ + \\ CH_2OHCHOHCH_2OH \end{array} \longrightarrow \begin{array}{c} H_2COSi(CH_3)_2R \\ | \\ HCOSi(CH_3)_2R + 3C_2H_5OH \\ | \\ H_2COSi(CH_3)_2R \end{array}$$
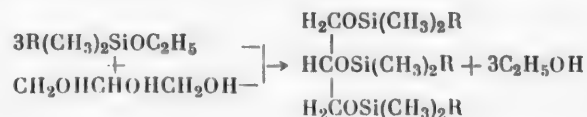
where R is CH_2Cl or $CHCl_2$.

The structures of the previously unknown tris (chloromethyldimethylsilyl) and tris(dichloromethyldimethylsilyl) triethers of glycerol was established by analysis and by a study of the hydrolysis products: bis (chloromethyl)-

Name and formula of ether	Yield, %	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Found, % C	Found, % H	Found, % Cl	Found, % Si	Calculated, % C	Calculated, % H	Calculated, % Cl	Calculated, % Si
Ethylene glycol bis(chloromethyl-dimethylsilyl) ether ClCH₂(CH₃)₂SiOCH₂CH₂OSi(CH₃)₂CH₂Cl	79	92—94°(5)	1.0729	1.4498	68.90	69.61	35.34, 35.33	7.10, 7.42	25.23, 25.42	20.30, 20.08	34.90	7.32	25.76	20.36
Ethylene glycol bis(dichloromethyl-dimethylsilyl) ether Cl₂CH(CH₃)₂SiOCH₂CH₂OSi(CH₃)₂CHCl₂	83	108—110 (2)	1.2244	1.4729	78.91	79.32	27.88, 27.83	5.48, 5.40	41.64, 41.57	15.97, 15.86	27.91	5.27	41.27	16.30
Glycerol tris(chloromethyldimethylsilyl) ether H₂C—OSi(CH₃)₂CH₂Cl HC—OSi(CH₃)₂CH₂Cl H₂C—OSi(CH₃)₂CH₂Cl	65	130—132 (6)	1.1108	1.4630	102.08	103.29	35.22, 35.16	7.12, 7.15	24.96, 24.78	19.95, 19.82	34.98	7.09	25.82	20.43
Glycerol tris(dichloromethyldimethyl-silyl) ether H₂C—OSi(CH₃)₂CHCl₂ HC—OSi(CH₃)₂CHCl₂ H₂C—OSi(CH₃)₂CHCl₂	72	140—142 (2)	1.2473	1.4821	117.73	117.95	28.90, 28.72	5.69, 5.52	40.87, 40.32	15.94, 15.89	27.97	5.09	41.28	16.33
Hydroquinone bis(chloromethyldimethyl-silyl) ether ClCH₂(CH₃)₂SiOC₆H₄OSi(CH₃)₂CH₂Cl	56	118—120 (2)	1.1417	1.5085	84.43	84.85	44.92, 44.85	6.58, 6.47	21.25, 21.42	16.88, 16.95	44.57	6.23	21.93	17.30
Ethylene glycol bis(ethoxydimethyl-silylmethyl) ether H₂COCH₂Si(CH₃)₂OC₂H₅ H₂COCH₂Si(CH₃)₂OC₂H₅	32	88—92 (4)	0.9231	1.4220	80.80	81.94	49.23, 49.08	10.92, 10.72	—	19.64, 19.44	48.94	10.26	—	19.05

tetramethyldisiloxane and bis (dichloromethyl) tetramethyldisiloxane were isolated, together with glycerol.

$$2 \quad \begin{array}{c} H_2COSi(CH_3)_2R \\ | \\ HCOSi(CH_3)_2R \\ | \\ H_2COSi(CH_3)_2R \end{array} + 3H_2O \longrightarrow \begin{array}{c} 3R(CH_3)_2SiOSi(CH_3)_2R \\ + \\ 2CH_2OHCHOHCH_2OH \end{array}$$
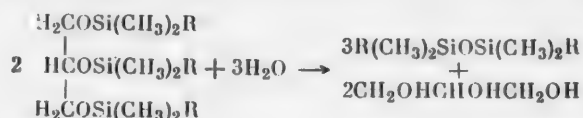
where R is CH_2Cl or $CHCl_2$.

Exchange etherification of chloromethyldimethylethoxysilane with hydroquinone took place in accordance with the reaction:

$$2ClCH_2(CH_3)_2SiOC_2H_5 + HOC_6H_4OH \longrightarrow$$
$$ClCH_2(CH_3)_2SiOC_6H_4OSi(CH_3)_2CH_2Cl + 2C_2H_5OH$$
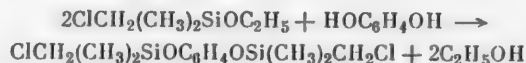
and ethyl alcohol and hydroquinone bis (chloromethyldimethylsilyl) ether were both formed in 56% yield.

The high yields showed that these exchange etherification reactions of chloromethylidimethylethoxysilane and dichloromethyldimethylethoxysilane took place by replacement of the alkoxy group, without any appreciable splitting of the chloromethyl and dichloromethyl groups.

However, in the reaction between chloromethyldimethylethoxysilane and sodium glycolate, there was preferential replacement of the chlorine atoms, without replacement of ethoxy by ethyleneoxy groups.

$$2ClCH_2(CH_3)_2SiOC_2H_5 + NaOCH_2CH_2ONa \xrightarrow[-2NaCl]{}$$
$$\longrightarrow C_2H_5O(CH_3)_2SiCH_2OCH_2CH_2OCH_2Si(CH_3)_2OC_2H_5$$
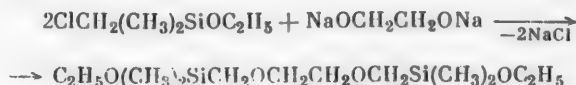
The properties of the new compounds are shown in the table.

EXPERIMENTAL

Chloromethyldimethylethoxy silane was obtained from chloromethyldimethylchlorosilane: b.p. 131-132°, n_D^{20} 1.4202, d_D^{20} 0.9508.

Dichloromethyldimethylethoxysilane was obtained from dichloromethyldimethylchlorosilane [3]: b.p. 162–163°, n_D^{20} 1.4408, d_4^{20} 1.0884.

Ethylene glycol bis (chloromethyldimethylsilyl) ether. Ethylene glycol (15.5 g = 0.25 mole) was heated with stirring in a spherical three-necked flask, fitted with a liquid-sealed stirrer, a thermometer, a dropping funnel, and a straight condenser with a receiver for condensate. Chloromethyldimethylethoxysilane (86 g = 0.56 mole) was added to the glycol at 100°. Alcohol was evolved during the addition, at the end of which the mixture was stirred for 2 hours at 120–130°. Distillation under reduced pressure then gave 54.5 g of product with a b.p. of 92–94°(5 mm).

Ethylene glycol bis (dichloromethyldimethylsilyl) ether was prepared in a similar way from dichloromethyldimethylethoxysilane.

Glycerol tris (chloromethyldimethylsilyl) ether was obtained similarly from 24 g (0.26) mole of glycerol and 135 g (0.89) mole of chloromethyldimethylethoxysilane. Distillation under reduced pressure gave 69.5 g of product, with a b.p. of 130–132° (6 mm).

Glycerol tris (dichloromethyldimethylsilyl) ether was obtained similarly from dichloromethyldimethylethoxysilane and glycerol.

Hydroquinone bis (chloromethyldimethylsilyl) ether was obtained similarly from 27 g (0.25 mole) of hydroquinone and 93 g (0.61 mole) of chloromethyldimethylethoxysilane. Distillation under reduced pressure gave 44.8 g of product, distilling at 118–120° (2 mm).

Ethylene glycol bis (ethoxydimethylsilylmethyl) ether. Metallic sodium (11.5 g) was stirred in a flask under 100 g of toluene and heated until molten. The temperature was adjusted to 100–105°, 15 g (0.26 mole) of ethylene glycol was added from a dropping funnel, and the mixture was maintained at this temperature for 30 minutes. The temperature was then reduced to 90–95°, and 76.5 g (0.5 mole) of chloromethyldimethylethoxysilane was

introduced from the dropping funnel. The sodium chloride deposited was filtered off after standing for 12 hours. The toluene was distilled off from the filtrate up to 120°, and the residue was redistilled under reduced pressure. The yield was 24 g of product, of b.p. 88—92° (4 mm).

The hydrolysis of ethylene glycol bis (chloromethyldimethylsilyl) ether. Water (50 g) and 0.2 ml of 0.1 N HCl were introduced into a three-necked flask fitted with a mechanical stirrer, a reflux condenser, a dropping funnel, and a thermometer. The ether (30 g = 0.11 mole) was added from the dropping funnel, with continuous stirring, over a period of 1 hour. The mixture was then heated for 1 hour at 50—60°. It separated into two layers on standing. The upper layer consisted of an aqueous solution of glycol. The lower layer was separated and distilled. The yield of bis (chloromethyl)-tetramethyldisiloxane [4] was 22 g.

B.p. 198—202°, n_D^{20} 1.4399, d_4^{20} 1.0424.

Found %: C 30.90, 30.74; H 6.76, 6.82; Si 23.88, 23.95. Calculated %: $C_6H_{16}OCl_2Si_2$. C 31.15; H 6.94; Si 24.31.

The hydrolysis of ethylene glycol bis (dichloromethyldimethylsilyl) ether was carried out similarly: 30 g (0.087 mole) of the ether gave 22 g of bis (dichloromethyl) tetramethyldisiloxane [5].

B.p. 117—119° (11 mm), n_D^{20} 1.4668, d_4^{20} 1.2205.

Found %: C 23.72, 23.65; H 4.62, 4.56; Si 18.43, 18.62. Calculated %: $C_6H_{14}OCl_4Si_2$. C 24.02; H 4.70; Si 18.72.

The glycerol tris (chloromethyldimethylsilyl) and tris (dichloromethyldimethylsilyl) ethers were hydrolyzed similarly, the products being glycerol and bis (chloromethyl)-and bis (dichloromethyl)-tetramethyldisiloxanes, whose composition and physical properties were the same as above.

SUMMARY

A study has been made of the reactions of exchange etherification of chloromethyldimethylethoxysilane and dichloromethyldimethylethoxysilane with ethylene glycol, glycerol and hydroquinone; five previously undescribed compounds were obtained and their properties were investigated. It was established that the exchange etherification reactions proceeded without appreciable splitting of the chloromethyl and dichloromethyl groups. The chlorine atom in chloromethyldimethylethoxysilane could be replaced by an ethyleneoxy group.

LITERATURE CITED

[1] M. M. Sprung, L. Nelson, J. Org. Ch. 20, 1750 (1955).

[2] J. L. Speier, J. Am. Chem. Soc. 71, 1474 (1949); K. A. Andrianov, L. I. Makarova, L. M. Volkova, and V. A. Odinets, Doklady Akad. Nauk SSSR 95, 269 (1954).

[3] K. A. Andrianov and M. A. Golubenko, Doklady Akad Nauk SSSR 112, 257 (1957).*

[4] R. H. Krieble, J. R. Elliott, J. Am. Chem. Soc. 67, 1810 (1945).

[5] R. H. Krieble and J. R. Elliott, J. Am. Chem. Soc. 68, 2291 (1946).

*Original Russian pagination. See C. B. Translation.

IMIDES OF AROMATIC SULFONIC ACIDS.
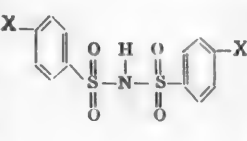
1. THE SYNTHESIS AND SOME PROPERTIES OF SYMMETRICAL AROMATIC SULFONIMIDES

N. N. Dykhanov

The imides of sulfonic acids have been less investigated than other organic sulfur compounds. The well known monograph by C. M. Suter only deals with N-substituted aromatic sulfonimides and their splitting under the influence of caustic alkali or ammonia [1]. Compounds of this series have been used for the synthesis of drugs, dyestuffs, tanning agents, and surfactants [2]. Those substituted at the nitrogen atom with nitrogen-containing heterocyclic radicals are of special interest, since it has been suggested that these should exhibit tautomerism [3], similar to that of the corresponding carboxylic acids, which has been established by means of their infrared spectra [4].

The synthesis of a simple aromatic sulfonimide—benzene sulfonimide—was first achieved in 1854 by Gerhardt, by the action of benzene sulfonyl chloride on the silver salt of benzene sulfonamide [6] The more readily available sodium salt was used later for the same purpose [6]. There is also a known method of obtaining symmetrical aryl sulfonimides by the action of 2 moles of aryl sulfonyl chloride on 1 mole of ammonia in aqueous solution [7]. Recently an original way of carrying out this reaction has been described, consisting in the simultaneous addition of an acetone solution of the sulfonyl chloride and of caustic alkali to an aqueous solution of ammonium chloride [8], which gives the symmetrical aryl sulfonimides in high yields.

In the course of a systematic investigation of aryl sulfonimides, we synthesized benzene sufonimide and a number of its symmetrical alkyl and halogeno para-substituted derivatives, by the action of a slight excess of the aryl sulfonyl chloride on the aryl sulfonamide in an aqueous solution of caustic alkali. • All the aryl sulfonimides obtained in this way differed from the amides of the same acids in showing strongly pronounced acidic properties: They liberated carbon dioxide from its salts and colored congo red like strong mineral acids; the pH of their saturated aqueous solutions was within the range 2—3. The regularities in the change of m.p. characteristic of para-halogeno substituted derivatives of benzene sulfonamide were not observed with the corresponding imides. The melting point of benzene sulfonamide is reduced by introduction of a fluorine atom into the para position, and then increases as the fluorine atom is replaced by halogen of increasing atomic weight, but the introduction of two similar halogen atoms into both the para positions of benzene sulfonimide always increased the melting point.

Compound	X	Melting point	Compound	X	Melting point
	H	154—155°		H	157—158°
	F	122—123		F	182—183
	Cl	143—144		Cl	207—208
	Br	165—166		Br	232—233
	I	182—183		I	250—251

•It will be shown in a subsequent paper that this method is also quite suitable for the synthesis of mixed aryl sulfoni-mides.

The increased acidic properties of aryl sulfonimides, as compared with aryl sulfonamides, can obviously be explained by the existence in the molecule of two positively charged sulfur atoms, which attract electrons from the nitrogen, and thus reduce its positive charge and facilitate ionization of the hydrogen linked to it. This property of aryl sulfonimides enables them to be used as reagents for separating individual organic bases from mixtures. In particular, by this means it was found possible to separate pure 2,6-lutidine from a mixture of pyridine homologs, since this is the strongest base in the so-called "beta-picoline" fraction from coal tar. The previous methods of isolating 2,6-lutidine are less effective [9].
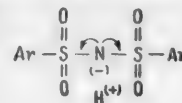
EXPERIMENTAL

1. Synthesis of the imides of aromatic sulfonic acids

A 5% solution of NaOH (880 ml) and 1 mole of recrystallized aryl sulfonamide were stirred and heated to 50—80° in a three-necked 3-liter flask, fitted with a stirrer and thermometer, and the liquid was maintained at this temperature while 1.1 mole of aryl sulfonyl chloride, which had been redistilled under reduced pressure, was added, a little at a time, over a period of 1—1.5 hours. • The medium was maintained weakly alkaline to bromothymol blue (pH about 7.2), throughout this time, by periodic addition of 5% NaOH. After the addition of all the sulfonyl chloride, the reaction mixture was stirred at the same temperature for 15—20 minutes, treated with 100 ml of 40% NaOH, and cooled to 15—20°. This caused the deposition of the crystalline sodium salt of the aryl sulfonimide in a yield of 30—95% (depending on its solubility). After 2—3 crystallizations from water and subsequent drying, first at 60—70° and then at 120—130°, the salts were free from impurities and contained no crystalline water; they were insoluble in the usual organic solvents (except for pyridine bases); they charred without melting on heating above 250°.

The free aryl sulfonimides were liberated from solutions of their sodium salts by addition of the calculated quantity of conc. HCl at 25—30°. Supplementary quantities of imides were obtained by acidification of the alkaline mother liquors, after the sodium salts had separated. The yields amounted to 70—98 %, based on the original amides. Pure imides were obtained from the technical products by recrystallization from water or alcohol. The pH of saturated aqueous solutions of the purified aryl sulfonimides (measured with universal indicator) varied between 2 and 3.

By this means we synthesized and characterized the sulfonimides of benzene (I), p-toluene (II), p-fluorobenzene (III), p-bromobenzene (IV), and p-iodobenzene (V), and also their sodium salts.

All the aryl sulfonimides obtained were white crystalline substances; they were insoluble in ether and other aromatic hydrocarbons; they were very soluble in acetone and pyridine, less so in water and alcohol (their solubilities in these last two solvents decreased markedly with increasing molecular weight).

Benzene sulfonimide. Starting materials: benzene sulfonamide and benzene sulfonyl chloride. Reaction temperature 50—55°. Yield 85—86%. Slightly soluble in cold water, readily soluble in alcohol, acetone, and pyridine; insoluble in ether and aromatic hydrocarbons; it crystallized from hot water (1:3) in the form of colorless hexahedral prisms, adhering in fan shaped agglomerates, with an m.p. of 157—158°.

Found %: C 48.61; H 3.80; N 4.66. Calculated %: $C_{12}H_{11}O_4NS_2$. C 48.48; H 3.73; N 4.71.

The Na salt was soluble in water (1:150 at 20°) and in pyridine; it crystallized from water (1:3) in the form of colorless plates.

Found %: C 45.01; H 3.10; N 4.40; Na 7.25. Calculated %: $C_{12}H_{10}O_4NS_2Na$. C 45.13; H 3.15 N 4.38; Na 7.20.

p-Toluene sulfonimide. Starting materials: p-toluene sulfonamide and p-toluene sulfonyl chloride. Reaction temperature 70—75°. Yield 81—82%. Sparingly soluble in cold water, readily soluble in alcohol, acetone, and pyridine, insoluble in ether and aromatic hydrocarbons; it crystallized from water (1:15) in the form of fine colorless needles, of m.p. 171—172°.

Found %: C 51.55; H 4.59; N 4.28. Calculated %: $C_{14}H_{15}O_4NS_2$. C 51.67; H 4.64; N 4.30.

•p-Fluoro-, bromo- and iodo-benzene sulfonyl chlorides were prepared similarly to p-chlorobenzene sulfonyl chloride [10], in yields of 58, 65, and 60%.

The Na salt was soluble in water (1:180 at 20°) and in pyridine; it crystallized from water (1:3) in the form of colorless leaflets.

Found %: C 48.42; H 4.01; N 4.10; Na 6.70. Calculated %: $C_{14}H_{14}O_4NS_2Na$. C 48.40; H 4.06; N 4.03; Na 6.62.

p-Bromobenzene sulfonimide. Starting materials: p-bromobenzene sulfonamide and p-bromobenzene sulfonyl chloride (m.p. 75—76°, b.p. 159—160° at 15—16 mm). Reaction temperature 75—78°. Yield 94—95%. Soluble in water (1:800 at 20°), soluble in alcohol, acetone, and pyridine, insoluble in ether and aromatic hydrocarbons; it crystallized from water (1:80) or alcohol (1:5) in the form of fine colorless needles, adhering in spherical agglomerates, of m.p. 232—233°.

Found %: C 31.70; H 2.00; N 3.00; Br 35.15. Calculated %: $C_{12}H_9O_4NS_2Br_2$. C 31.66; H 11.99; N 3.07; Br 35.11.

The Na salt was soluble in water (1:500 at 20°) and pyridine; it crystallized from hot water (1:15) in the form of fine colorless rods.

Found %: C 30.29; H 1.70; Br 33.52; Na 4.91. Calculated %: $C_{12}H_8O_4NS_2Br_2Na$. C 30.20; H 1.69; Br 33.49; Na 4.82.

p-Iodobenzene sulfonimide. Starting materials: p-iodobenzene sulfonamide and p-iodobenzene sulfonyl chloride (m.p. 86—87°, b.p. 150-151.5° at 5—6 mm). Reaction temperature 85—90°. Yield 97—98%. Soluble in water (1:1000 at 20°), readily soluble in alcohol, acetone and pyridine, insoluble in ether and aromatic hydrocarbons; it crystallized from alcohol (1:10) in the form of fine colorless needles, of m.p. 250—251°.

Found %: C 26.09; H 1.72; N 2.65; I 45.98. Calculated %: $C_{12}H_9O_4NS_2I_2$. C 26.24; H 1.65; N 2.55; I 46.02.

The Na salt was soluble in water (1:800 at 20°) and pyridine; it crystallized from water (1:25) in the form of fine colorless rods.

Found %: C 25.29; H 1.45; I 44.40; Na 4.00. Calculated %: $C_{12}H_8O_4NS_2I_2Na$. C 25.23; H 1.41; I 44.44; Na 4.02.

p-Fluorobenzene sulfonimide. Starting materials: p-fluorobenzene sulfonamide and p-fluorobenzene sulfonyl chloride (m.p. 35—36°, b.p. 87—89° at 3 mm). Reaction temperature 55—60°. Yield 70—72%. Soluble in water (1:200 at 20°) and pyridine, readily soluble in alcohol and acetone, insoluble in ether and aromatic hydrocarbons; it crystallized from water (1:15) or from alcohol (1:3) in the form of fine colorless needles, of m.p. 182—183°.

Found %: C 43.27; H 2.79; N 4.16; F 11.29. Calculated %: $C_{12}H_9O_4NS_2F_2$. C 43.23; H 2.72; N 4.20; F 11.40.

The Na salt was soluble in water (1:150 at 20°) and in pyridine; it crystallized from hot water (1:3) in the form of fine colorless leaflets.

Found %: C 40.59; H 2.32; F 10.60; Na 6.44. Calculated %: $C_{12}H_8O_4NS_2F_2Na$. C 40.57; H 2.27; F 10.69; Na 6.47.

2. The isolation of 2,6-lutidine from the "beta-picoline" fraction of pyridine bases by means of benzene sulfonimide.

A 100 g sample of coal tar pyridine bases, boiling in the range 138—146° (the "beta-picoline" fraction), and 25 g of benzene sulfonimide, were placed in a 150 ml flask fitted with a thermometer and a reflux condenser. The resulting suspension was heated until the imide dissolved (100—120°), maintained at this temperature for 30 minutes, and then cooled to 15—20°. The deposit formed was filtered off, washed with 50 ml of ether, pressed out, and dried to constant weight at 75—80°. The yield was 28—30 g.

The salt of 2,6-lutidine with benzene sulfonimide was readily soluble in water in the cold, and dissolved in alcohol, acetone, and pyridine on heating; it was insoluble in ether or aromatic hydrocarbons; it crystallized from alcohol (1:5) in the form of fine colorless needles, of m.p. 169.5—171°.

Found %: C 56.50; H 5.00; N 6.89. Calculated %: $C_{19}H_{20}O_4N_2S_2$. C 56.41; H 4.98; N 6.92.

The salt (200 g) was added to 1 liter of 5% caustic soda and heated to 90—100°, and 2,6-lutidine was distilled off in steam from the resulting solution; the end of the distillation was determined by the absence of an organic layer when excess of solid sodium hydroxide was added to a sample of the distillate. The 350—400 ml of distillate, containing the 2,6-lutidine, was treated with 20 g of solid caustic soda for every 100 ml of distillate. The upper organic layer was separated, dried over solid NaOH, and distilled. The yield was 40—44 g of 2,6-lutidine, b.p. 143—143.5°; picrate, m.p. 161—162°. The residue, after distilling of the 2,6-lutidine, was neutralized with conc. HCl. The deposit was filtered off, washed with a small quantity of cold water, and dried. The product was 130—135 g of the original benzene sulfonimide.

SUMMARY

1. A general method is described for the synthesis of aryl sulfonimides by the interaction of aryl sulfonamides with aryl sulfonyl chlorides in an alkaline aqueous medium. The imides of p-fluoro-,p-bromo- and p-iodo-benzene sulfonic acids, and their sodium salts, have been obtained for the first time, and the imides of benzene and p-toluene sulfonic acids have been characterized.

2. A new method is presented for isolating 2,6-lutidine, as its benzene sulfonimide salt, from a mixture with other pyridine homologs.

LITERATURE CITED

[1] C. M. Suter, The Organic Chemistry of Sulfur, Part III [Russian translation] (IL, 1951) p. 15.

[2] N. N. Dykhanov, Author's Certificate 2532 (1956); German Patent 3289 (1953).

[3] B. G. Yasnitskii and E. B. Dol'berg, Zhur. Obschei Khim. 26, 2046 (1956). *

[4] V. V. Kushkin and I Ya. Postovskii, Doklady Akad. Nauk. SSSR 83, 63 (1953); S. G. Bogomolov, Yu. N. Sheinker and I. Ya. Postovskii, Doklady Akad. Nauk SSSR 98 (1953).

[5] Gerhardt, Traité de chim. org. III, 75 (1854); Beilst. 11, 49 (1928).

[6] German Patent 125390; Zbl. 1901, II, 1185; M. V. Rubtsov, Zhur. Obschei Khim. 10, 839 (1940).

[7] L. M. Crossley, E. H. Northey, and M. E. Hultquist, J. Am. Chem. Soc. 60, 2222 (1938).

[8] F. Runge, H.-J. Engelbrecht, and G. Preusser, Ber. 86, 1571 (1953).

[9] A. M. Grigorovskii and Z. M. Kimen, Zhur. Priklad. Khim. 18, 259 (1940).

[10] A. M. Grigorovskii, N. N. Dykhanov, and Z. M. Kimen, Zhur. Priklad. Khim. 28, 616 (1955).*

* Original Russian pagination. See C. B. Translation.

CYANINE DYES WITH UNSATURATED SUBSTITUENTS.

V. DIMETHINEMEROCYANINES. RHODANINE DERIVATIVES
WITH UNSATURATED SUBSTITUENTS IN THE BENZTHIAZOLE RING

M. A. Al'perovich, I. K. Ushenko, L. N. Tyurina, and M. K. Grechko

The Affiliated Scientific Research Kinophoto Institute at Factory No. 3 and the

Institute of Organic Chemistry of the Academy of Sciences of the Ukrainian SSR

Descriptions have recently appeared in the literature of various dimethinemerocyanines, and their optical and photographic properties have been investigated [1,4]. Such dyes are quite effective as optical sensitizers for photographic emulsions [2] and are also of interest from the point of view of the theory of color of organic compounds, since they are internally ionized compounds, whose molecules can exist either in the nonpolar form A, or in the form of a bipolar ion B:

(A)   (B)

Y=O, S, Se or —CH=CH—
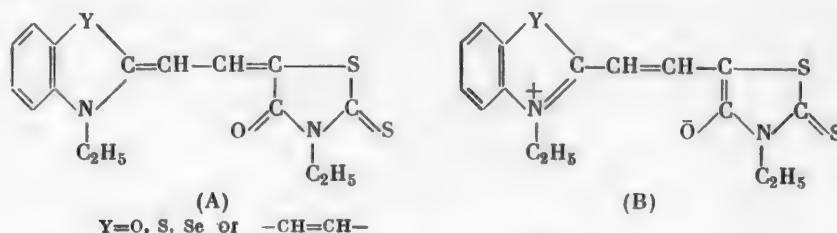
These dyes are more or less covalent in structure, depending on the composition of their heterocyclic nitrogen-containing rings [3,4]. If the merocyanine structure is intermediate between the internally ionized and covalent forms, which corresponds to the most equilibrium distribution of electron density along the polymethine chromophore, then the absorption maximum should clearly coincide with the arithmetic mean of the absorption maxima corresponding to the symmetrical carbocyanine and the monomethineoxanine [4—7]. When the actual structure of a merocyanine molecule deviates toward the covalent form, its absorption maximum must be displaced toward shorter wavelength, as compared with the mean calculated value, so that the extent of this hypsochromic shift will be greater, the less the basicity of the heterocyclic nitrogen-containing ring [3,4].

In this paper we present the results of an investigation of the optical properties of dimethinemerocyanines, derivatives of 3-ethylrhodanine, with the following substituents in the benzthiazole or quinoline ring systems: styryl, p-methylstyryl, p-methoxystyryl, p-nitrostyryl, and ω-phenylbutadienyl. Such dyes have not been described in the literature.

The dimethinemerocyanines were obtained by the interaction of 3-ethyl-5-(acetanilidomethylene) rhodanine with the quaternary salts of 2-methylbenzthiazole or of quinaldine, containing the unsaturated substituents in the benzthiazole or quinoline ring systems. The condensation was carried out in pyridine or in anhydrous alcohol, in the presence of triethylamine [2], for example:

$$C_6H_5-CH=CH- \quad \text{(benzthiazole)} \quad C-CH_3 \; + \; COCH_3 / N-CH=C-S \text{(rhodanine)} \rightarrow$$

$$C_6H_5-CH=CH- \quad C=CH-CH=C-S \text{(merocyanine)}$$

$$B \begin{cases} \\ \end{cases} \quad C=CH-CH=C-S$$
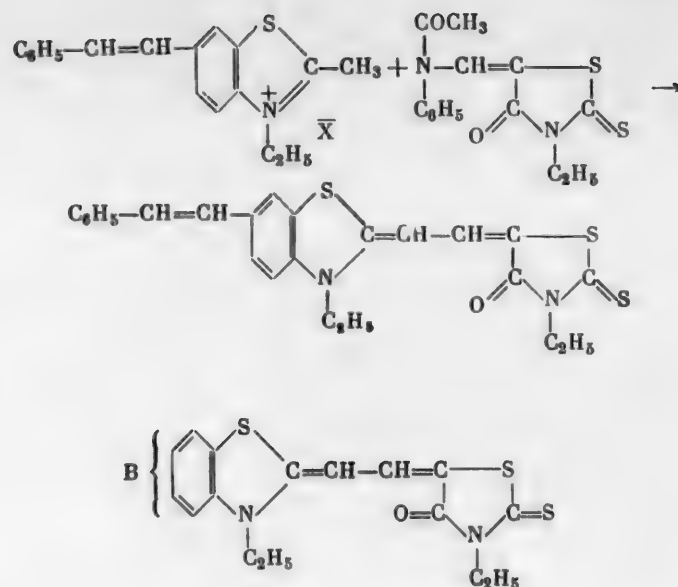
TABLE 1

Compound no.	B	Substituent position	Absorption maximum, $m\mu$	Hypsochromic shift, $m\mu$
I	$C_6H_5-CH=CH-$		531	28
II	$CH_3-\bigcirc-CH=CH-$		535	26
III	$CH_3O-\bigcirc-CH=CH-$	5	533	28
IV	$O_2N-\bigcirc-CH=CH-$		529	29
V	$C_6H_5-[CH=CH]_2-$		533	33
VI	$C_6H_5-CH=CH-$		540	27.5
VII	$CH_3-\bigcirc-CH=CH-$		541	29
VIII	$CH_3O-\bigcirc-CH=CH-$	6	543	29.5
IX	$O_2N-\bigcirc-CH=CH-$		545	27.5
X	$C_6H_5-[CH=CH]_2-$		545	30.5

Table 1 shows the positions of the absorption maxima of alcohol solutions of the merocyanines obtained, and their hypsochromic shifts from the values calculated from the positions of the absorption maxima of the corresponding carbocyanines and monomethineoxanines, which are at about 540 mμ in alcohol [4].

The introduction of unsaturated substituents into the benzthiazole or quinoline ring systems of a merocyanine was found to produce a displacement of the absorption maximum towards longer wavelength. There was a smaller bathochromic effect by unsaturated substituents in the 5-position than by those in the 6-position. It should be noted that the bathochromic shift, produced, for example, by the introduction of a styryl group into the 6-position of a merocyanine, was somewhat less than in the case of a carbocyanine (15 instead of 22). This is evidently related to the fact that, in this type of dyestuff, there is only a slight electron displacement from the heterocyclic nitrogen atom to the oxygen of the rhodanine ring, which is the reason for the lower degree of conjugation of the styryl group with the main polymethine chromophore.
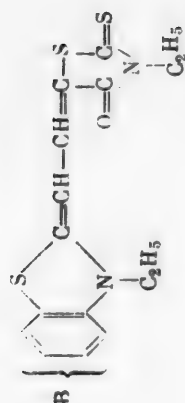
TABLE 2

B	Position of substituent	Absorption maximum, mμ							
		CH₃OH ε 31.2	C₂H₅OH ε 25.8	C₃H₇OH ε 22.2	C₄H₉OH ε 17.7	CHCl₃ ε 4.64	C₆H₆ ε 2.29	CCl₄ ε 2.19	C₇H₁₆ ε 1.91
H	—	524	524	522 (−2)*	524	523 (−1)	513 (−11)	504 (−20)	490 (−34)
C₆H₅—CH=CH—	5	534	531 (−3)	532 (−2)	531 (−3)	526 (−8)	520 (−14)	514 (−20)	496 (−38)
CH₃—CH=CH—		534	535 (+1)	534 (0)	530 (−4)	532 (−2)	519 (−15)	513 (−21)	497 (−37)
CH₃O—CH=CH—		532	533 (+1)	534 (+2)	534 (+2)	532 (0)	521 (−11)	514 (−18)	500 (−32)
O₂N—CH=CH—		534	533 (−1)	536 (+2)	533 (−1)	531 (−3)	517 (−17)	513 (−21)	—
C₆H₅—[CH=CH]₂—		535	533 (−2)	534 (−1)	533 (−2)	533 (−2)	520 (−15)	514 (−21)	499 (−36)
C₆H₅—CH=CH—	6	539	538 (−1)	540 (+1)	538 (−1)	543 (+4)	530 (−9)	518 (−21)	505 (−34)
CH₃—CH=CH—		543	541 (−2)	544 (+1)	542 (−1)	540 (−3)	528 (−15)	522 (−21)	506 (−35)
CH₃O—CH=CH—		544	543 (−1)	544 (0)	542 (−2)	540 (−4)	529 (−15)	522 (−22)	508 (−35)
O₂N—CH=CH—		544	545 (+1)	543 (−1)	542 (−2)	543 (−1)	532 (−12)	522 (−22)	—
C₆H₅—[CH=CH]₂—		544	545 (+1)	542 (−2)	542 (−2)	541 (−3)	533 (−11)	524 (−20)	510 (−34)

*The figures in brackets are the shifts in the positions of the absorption maxima in the given solvent relative to their positions in methanol.

3569

TABLE 3

Compound no.	Name of dye	Starting material, g		Solvent		Et₃N, ml	Amount of solvent for crystallization, ml	Yield, %	Melting point	% N, found	Calculated (empirical formula)	% N
		A	quaternary salt, g	name	ml							
I	3-Ethyl-5-(3'-ethyl-5'-styryl-benzthiazolinyl-2'-vinylene)-4-oxo-2-thiothiazolidine	0.3	0.45-C	Alcohol	6	0.14	Glacial acetic acid 55	54.5	251—252°	6.19, 6.20	$C_{24}H_{22}ON_2S_3$	6.21
II	3-Ethyl-5-(3'-ethyl-5'-p-methyl-styrylbenzthiazolinyl-2'-vinylene)-4-oxo-2-thiothiazolidine	0.3	0.48-E	"	6	0.14	Benzene,10	54.4	280—282	5.90, 6.05	$C_{25}H_{24}ON_2S_3$	6.03
III	3-Ethyl-5-(3'-ethyl-5'-p-methoxystyrylbenzthiazolinyl-2'-vinylene)-4-oxo-2-thiothiazolidine	0.3	0.49-G	"	6	0.14	Benzene,120	12.5	260—262	5.67, 5.57	$C_{25}H_{24}O_2N_2S_3$	5.82
IV	3-Ethyl-5-(3'-ethyl-5'-p-nitro-styrylbenzthiazolinyl-2'-vinyl-ene)-4-oxo-2-thiothiazolidine	0.3	0.39-I	"	6	0.14	Benzene 300	59	264—266	8.38, 8.49	$C_{24}H_{21}O_3N_3S_3$	8.47
V	3-Ethyl-5-(3'-ethyl-5'-8-phenyl-butadienylbenzthiazolinyl-2'-vinylene)-4-oxo-2-thiothiazolidine	0.3	0.47-K	"	6	0.14	Benzene 100	27	291—293	5.78, 5.69	$C_{26}H_{24}ON_2S_3$	5.89

TABLE 3 (continued)

Compound no.	Name of dye	Starting material, g		Solvent		Tri-ethyl-amine, ml	Amount of solvent for crystalliza-tion, ml	Yield %	Melting point	% N found	Calculated (empirical formula)	% N
		A	quarter-nary salt	name	ml							
VI	3-Ethyl-5-(3'-ethyl-6'-styryl-benzthiazolinyl-2'-vinylene)-4-oxo-2-thiothiazolidine	0.3	0.45-B	Pyridine	3	—	Pyridine 3	51	239—240	5.96, 5.88	$C_{21}H_{28}ON_2S_3$	6.21
VII	3-Ethyl-5-(3'-ethyl-6'-p-methyl-styrylbenzthiazolinyl-2'-vinyl-ene)-4-oxo-2-thiothiazolidine	0.3	0.48-D	Alcohol	6	0.14	Benzene 300	36	259	6.12, 6.02	$C_{25}H_{24}ON_2S_3$	6.03
VIII	3-Ethyl-5-(3'-ethyl-6'-p-methoxystyrylbenzthiazolinyl-2'-vinylene)-4-oxo-2-thiothiazolidine	0.3	0.49-F	Pyridine	3	—	Benzene 50	41	250—251	5.78, 5.60	$C_{25}H_{24}O_2N_2S_3$	5.82
IX	3-Ethyl-5-(3'-ethyl-6'-p-nitro-styrylbenzthiazolinyl-2'-vinyl-ene)-4-oxo-2-thiothiazolidine	0.3	0.39-H	Alcohol	6	0.14	Benzene 300	18	292—293	8.12, 8.26	$C_{24}H_{21}O_3N_3S_3$	8.47
X	3-Ethyl-5-(3'-ethyl-6'-8-phenyl-butadienylbenzthiazolinyl-2'-vinylene)-4-oxo-2-thiothiazolidine	0.3	0.47-J	Ditto	6	0.14	Benzene 100	40	215—216	5.78, 5.69	$C_{26}H_{24}ON_2S_3$	5.89

The hypsochromic shifts of the absorption maxima of merocyanines with unsaturated substituents are only very slightly greater than those for the unsubstituted dyes. It would therefore be anticipated that the introduction of unsaturated groupings into the benzthiazole or quinoline ring systems would only have a slight effect on the distribution of electron density in the polymethine chromophore of a dimethinemerocyanine. But the observed tendency to a slight increase in the hypsochromic shift indicates that the unsaturated groupings reduce the basicity of the heterocyclic systems, and consequently promote a weak electron-acceptor character in this type of dye.

It is known that deepening of color with solvation is a characteristic phenomenon with merocyanine and other internally ionized dyes. Solutions of merocyanines in polar solvents (alcohols) normally have a deeper color than solutions in nonpolar solvents (benzene, hexane). The solvent polarity influences the distribution of electron density in the molecule and consequently the color of an internally ionized dye [6,8,9]. We therefore determined the absorption maxima of dimethinemerocyanines in solvents of different polarity (Table 2).

The absorption maxima of dimethinemerocyanines shifted gradually to shorter wave length on changing from methanol to less polar solvents. This indicated that the structures of these dyes in solution approximated more closely to the covalent form A [9], on changing from methanol to less polar solvents.

EXPERIMENTAL

Synthesis of bases and quaternary salts. 2-Methylbenzthiazoles and quinaldines containing unsaturated substituents, and also their quaternary salts, were obtained by our previously described methods [10].

Merocyanines. The method of synthesis was general. A quaternary salt was dissolved in anhydrous alcohol or pyridine. 3-Ethyl-5-(acetanilidomethylene)-rhodanine and triethylamine were added to the solution, and the mixture was boiled for a few minutes. The dyestuff deposited was filtered off, washed with alcohol, and recrystallized to constant melting point. In some cases, preliminary chromatography on aluminum oxide was applied to the benzene solution. The merocyanines were obtained as violet prisms or green platelets. Table 3 shows the conditions of synthesis and analytical results for the merocyanines.

The following letters are used to denote the various starting materials: A) 3-ethyl-5-(acetanilidomethylene)-rhodanine; B) the ethyl p-toluene sulfonates of 2-methyl-6-styrylbenzthiazole, C) 2-methyl-5-styrylbenzthiazole, D) 2-methyl-6-p-methylstyrylbenzthiazole, E) 2-methyl-5-p-methyl-styrylbenzthiazole, F) 2-methyl-6-p-methoxy-styrylbenzthiazole, G) 2-methyl-5-p-methoxystyrylbenzthiazole, H) 2-methyl-6-p-nitrostyrylbenzthiazole, I) 2-methyl-5-p-nitrostyrylbenzthiazole, J) 2-methyl-6-γ-phenylbutadienyl benzthiazole , and K) 2-methyl-5-γ-phenyl-butadienylbenzthiazole.

3,3'-Diethyl-6-styrylthiacarbocyanine iodide (XI) A mixture of 0.45 g of the ethyl p-toluene sulfonate of 2-methyl-6-styrylbenzthiazole, 0.45 g of the ethyl iodide of 2-(acetanilidovinyl) benzthiazole, 3 ml of pyridine, and 0.05 g of acetic anhydride was boiled for 15 minutes. The dyestuff deposited and was washed with 45 ml of ether. It was dissolved in 10 ml of boiling alcohol, and its iodide was precipitated by addition of an aqueous solution of potassium iodide. The oily product crystallized on grinding with 40 ml of ether. It was recrystallized from 170 ml of alcohol. The yield was 0.19 g (32 %). M.p. 188-190°.

Found %: S 10.24, 10.22. Calculated %: $C_{29}H_{27}N_2S_2I$. S 10.77.

SUMMARY

1. Ten dimethinemerocyanines have been prepared, containing styryl and ω-phenylbutadienyl substituents in the benzthiazole ring system.

2. It has been found that the introduction of an unsaturated substituent into the merocyanine molecule produces a displacement of the absorption maximum toward. longer wave length.

3. The positions of the dimethinemerocyanine absorption maxima have been determined in solvents of different polarity, and it has been found that there is a continuous displacement of the maximum towards shorter wave length with change of solvent from methanol to benzene.

LITERATURE CITED

[1] M. V. Deichmeister, I. I. Levkoev, and É. B. Lifshits, Zhur. Obschei Khim. 23, 1529 (1953);* Zhur. Obschei Khim. 27, 202 (1957);* I. I. Levkoev, Z. P. Sytnik, and S. V. Natanson, Uspekhi Nauchnoi Fotografii 2, 11 (1953).

[2] French Patent 793722; British Patents 450598 and 466244.

[3] L. Brooker, Frontiers in Chemistry, III 63 (1945).

[4] M. V. Deichmeister, Z. P. Sytnik, and É. B. Lifshits, Zhur. Obschei Khim. 22, 166 (1952).*

[5] A. I. Kiprianov and G. T. Pilyugin, Uchenye Zapiski Kharkov. Gosudarst. Univ. 10, 104 (1937); A. I. Kiprianov and V. E. Petrun'kin, Zhur. Obschei. Khim. 10, 613 (1940); A. I. Kiprianov, Yubil. Sbornik Akad. Nauk Ukr. SSR 1, 254 (1944).

[6] A. I. Kiprianov and E. S. Timoshenko, Zhur. Obschei Khim. 17, 1468 (1947).

[7] N. N. Sveshnikov, I. I. Levkoev, and V. V. Durmashkina, Zhur. Obschei Khim. 14, 198 (1944).

[8] M. V. Deichmeister, I. I. Levkoev, and É. B. Lifshits, Zhur. Obschei Khim. 23, 1532 (1953).

[9] I. I. Levkoev, N. N. Sveshnikov, and É. B. Lifshits, Doklady Akad. Nauk SSR 74, 275 (1950).

[10] M. A. Al'perovich, I. K. Ushenko, and L. I. Tyurina, Zhur. Obschei Khim. 28, 2538 (1958);* Zhur. Obschei Khim. 29, 3376 (1959);* I. K. Ushenko and S. E. Gornostaeva, Zhur. Obschei Khim. 28, 1668 (1958);* M. A. Al'perovich and I. K. Ushenko, Zhur. Obschei Khim. 29, 3384 (1959).*

---

*Original Russian pagination. See C. B. Translation.

AMINES WITH GANGLIOLYTIC ACTIVITY

I. AMINES OF THE CYCLOPENTANE AND CYCLOHEXANE SERIES

N. K. Kochetkov, A. Ya. Khorlin, K. I. Lopatina, and L. A. Vorotnikova

Institute of Pharmacology and Chemotherapy of the Academy of Medical Sciences of the USSR

The recently discovered gangliolytic activity of compounds of the 3-alkylaminoisocamphane series [1,2], including a highly active preparation with prolonged ganglionic-blocking action (mecamine or Inversine [1], indicates that high gangliolytic activity is inherent not only in quaternary ammonium salts but also in amines. Investigations in our laboratory [2] brough to light several correlations of physiological activity with the structure of 3-alkylaminoisocamphanes. It was shown that only secondary amines are appreciably active and that a condition for high activity is that one of the radicals attached to the nitrogen should be methyl or ethyl. Concerning the specific action of the remainder of the molecule, it was still not clear to what extent presence of a complex bicyclic radical was necessary for high gangliolytic activity.

With the objective of solving this problem, we synthesized some alicyclic amines of the cyclopentane and cyclohexane series of the type of (IV). These products contain some of the structural features of mecamine [(I), $R = CH_3$]. The following steps were involved in the synthesis:
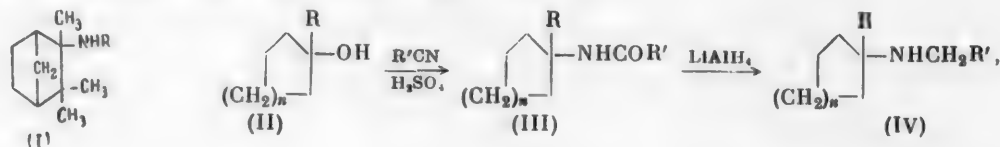
where $R = CH_3$, C_2H_5, $n-C_3H_7$, $n-C_4H_9$; $R' = H$, CH_3; $n = 1,2$.

We synthesized acylamines (III) with the help of the Ritter reaction [3] which is a uniquely convenient method of synthesis of amides with highly branched radicals attached to the nitrogen, including tertiary amides (so-called carbinamides). This reaction has been extensively investigated in recent years [4] and has made carbinamides and in turn carbinamines easily accessible compounds; among the latter were found compounds with spasmolytic activity [5].

For the nitrile components of the amidic condensation we selected hydrocyanic acid (R' = H) and acetonitrile (R' = CH_3), since we had shown in the case of synthesis of mecamine analogs [2] that compounds containing methyl [(I), R = CH_3] and ethyl (R = C_2H_5) groups possess the strongest gangliolytic activity.

For investigation of the influence of the nature of radical R and of the size of the alicyclic ring on the physiological activity of amines (IV), the appropriate tertiary alcohols of the cyclopentane and cyclohexane series were converted into:1-methyl-, 1-ethyl-, 1-n-propyl-, 1-n-butyl -1-acetamidocyclopentanes; 1-methyl-and 1-ethyl-1-formamidocyclopentanes; 1-methyl-, 1-ethyl and 1-n-propyl-1-acetamidocyclohexanes; and 1-ethyl-1-formamidocyclohexane. Tertiary alcohols (II) were condensed with acetonitrile and hydrocyanic acid under the usual conditions of the Ritter reaction, i.e. in the presence of concentrated sulfuric acid.

Tertiary alcohols react with acetonitrile equally smoothly in a medium of dibutyl ether or of glacial acetic acid. We obtained the best results, however, in the absence of a solvent and with use of a two-fold excess of acetonitrile (in relation to the alcohol) and of a suitable quantity of concentrated sulfuric acid. 1-Ethylcyclopentanol

and 1-ethylcycloxanol were condensed with hydrocyanic acid in propionic acid solution.

The resulting substituted acetamides [(III), R' = CH₃] are colorless, crystalline substances, readily soluble in the majority of organic solvents and difficultly soluble in ligroine. The substituted formamides [(III), R = CH₃, C₂H₅; R' = H] have low melting points; they were therefore purified by vacuum distillation.

Amides (III) were subsequently reduced to 1-alkyl-1-alkylaminocycloalkanes (IV) with the help of lithium aluminum hydride; optimum results were obtained with a 1.5- to 2-fold excess of the reducing agent. Amines (IV) were isolated and purified in the form of their hydrochlorides; the latter were prepared by reaction of the bases with hydrogen chloride in ether. The hydrochlorides of 1-ethyl-1-methylaminocyclopentane and 1-ethyl-1-ethylaminocyclohexane were extremely hygroscopic; in these cases the bases were therefore converted to the acid oxalates by the action of an ethereal solution of anhydrous oxalic acid.

All of the amines (IV) that were prepared were tested for their gangliolytic activity by Yu. V. Uranov. The results of these tests show that the majority of the compounds exert gangliolytic activity in doses of the order of 10 mg/kg. The most active preparation of this series is ethyl-(1-ethylcyclopentyl)-amine [(IV), n = 1, R = C₂H₅]. The activity is halved when the ethyl radical is replaced by methyl [(IV), n = 1, R = CH₃], and it virtually disappears when larger radicals are introduced [(IV), n = 1, R = n-C₃H₇ or n-C₄H₉]. Amines of the cyclohexane series are generally less active. For example, [(IV, n = 2, R = CH₃] is nearly inactive, whereas its ethyl analog is active but not as active as the cyclopentyl analog.

These observations show that the presence of the bicyclic isocamphane structure is not essential for the development of ganglion-blocking activity in secondary amines. At the same time a rigid conformation of the alicyclic ring appears to be an important factor.

EXPERIMENTAL

The starting tertiary alcohols were synthesized from cyclopentanone or cyclohexanone and the appropriate alkylmagnesium halide by the known procedures.

1-Alkyl-1-acetamidocycloalkanes [(III), R' = CH₃]. To a mixture of 0.1 mole alcohol and 0.2 mole acetonitrile was added in small portions (with stirring and cooling) 0.2 mole of 98% sulfuric acid, the temperature being held at not higher than 40°. After it had been kept for 24 hr at room temperature, the reaction mass was poured onto ice and neutralized with 10% ammonia. The resulting crystalline amides were purified by recrystallization from a mixture of benzene and ligroine or by sublimation in vacuo at 70—80° (2 mm). Yields, constants, and analytical data of the resulting N-substituted acetamides are presented in Table 1.

TABLE 1

Synthesis of Amides

(III)
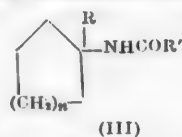
No.	n	R	R'	Yield (in %)	Melting point	Boiling point (mm Hg)	Found N (%)	Empirical formula	Calc. N (%)
1		CH₃		57	98—99°	—	9.72, 9.71	$C_8H_{15}ON$	9.92
2	1	C₂H₅	CH₃	36	86—87	—	9.02, 9.14	$C_9H_{17}ON$	9.02
3		n-C₃H₇		59	111—111.5	—	8.50, 8.51	$C_{10}H_{19}ON$	8.27
4		n-C₄H₉		25	89—90	—	7.35, 7.53	$C_{11}H_{21}ON$	7.64
5		C₂H₅	H	82	—	128—130°(5)	10.02, 9.90	$C_8H_{15}ON$	9.92
6		CH₃		35	83—84	—	8.91, 8.72	$C_9H_{17}ON$	9.02
7	2	C₂H₅	CH₃	65	71—72	—	8.54, 8.56	$C_{10}H_{19}ON$	8.27
8		n-C₃H₇		72	69—70	—	7.37, 7.56	$C_{11}H_{21}ON$	7.64
9		C₂H₅	H	65	—	130—132(3)	9.10, 9.15	$C_9H_{17}ON$	9.02

TABLE 2

Synthesis of Amines

$$\text{(CH}_2)_n - \overset{\displaystyle R}{\underset{\displaystyle }{\text{C}}} - \text{NHCH}_2\text{R}' \cdot \text{HX}$$
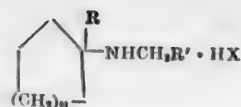
No.	n	R	R'	X	Yield (in %)	Melting point	Found (%)	Empirical formula	Calculated (%)
1	1	CH_3	CH_3	Cl	65	184—185°	20.96	$C_8H_{18}NCl$	20.93
2		C_2H_5			61	193—194	19.68, 19.62	$C_9H_{20}NCl$	19.95
3		$n\text{-}C_3H_7$			52	154—155	18.61, 18.62	$C_{10}H_{22}NCl$	18.43
4		$n\text{-}C_4H_9$			60	147—148	17.20, 17.25	$C_{11}H_{24}NCl$	17.24
5	2	CH_3			59	203—204	20.02, 20.17	$C_9H_{20}NCl$	19.95
6		C_2H_5			60	193—194	18.55, 18.68	$C_{10}H_{22}NCl$	18.43
7		$n\text{-}C_3H_7$			58	191—192	17.26, 17.12	$C_{11}H_{24}NCl$	17.24
8	1	C_2H_5	H	C_2O_4H	60	163—164	55.76, 55.78; 8.83, 9.00	$C_{11}H_{19}O_4N$	55.27, 8.81
9	2	C_2H_5	H	C_2O_4H	57	173—174	57.81, 57.80; 9.30, 9.40	$C_{11}H_{21}O_4N$	57.11, 9.15

Note. Cl content given in expts. 1-7, and C and H contents in expts. 8 and 9.

1-Ethyl-1-formamidocycloalkanes [(III), R' = H]. To a suspension of 0.2 mole potassium cyanide in a solution of 0.1 mole alcohol in 20 ml propionic acid was added dropwise, with intensive stirring, 0.3 mole of 98% sulfuric acid. The temperature of the mixture was kept at not higher than 10° during the operation. After the reaction mass had been kept for 24 hr at room temperature, it was poured onto ice and neutralized with ammonia. An oil separated and was extracted with benzene and distilled in vacuo. Yield, constants, and analytical data are presented in Table 1.

Hydrochlorides of 1-alkyl-1-alkylaminocycloalkanes (IV). 0.05 mole of amide (III) was added to a solution of 0.08 mole lithium aluminum hydride (from 0.08 mole aluminum bromide and 0.32 mole lithium hydride) in 50 ml absolute ether. The mixture was then stirred at the boil for 4 hr. 100 ml 30% NaOH was then run in (ice cooling); the ether layer was collected; the aqueous layer was extracted twice with ether, and the combined ether extracts were dried with solid alkali, and filtered; the solution was then concentrated to a volume of 15—20 ml by distillation of solvent. To the remaining ethereal solution of amine was added (with cooling) an ethereal solution of hydrogen chloride until the amine hydrochloride had been completely precipitated (alternatively the ethereal solution of the amine was added to an ethereal solution of anhydrous oxalic acid). The precipitated crystals of hydrochloride or acid oxalate were filtered, washed on the filter with absolute ether and dried in a vacuum-desiccator. Yields, constants, and analytical data for the salts of amines (IV) are presented in Table 2.

SUMMARY

1. Interaction of 1-alkyl-1-cyclopentanols and 1-alkyl-1-cyclohexanols with acetonitrile and with hydrogen cyanide by the Ritter reaction and subsequent reduction of the amides with lithium aluminum hydride gave a series of 1-alkylcyclopentyl- and 1-alkylcyclohexyl-1-alkylamines.

2. Tests of the prepared compounds for ganglion-blocking activity show that the presence of the isocamphane skeleton is not an essential condition for the manifestation of ganglion-blocking activity by secondary amines.

3. Some data for the relation between physiological activity and structure of the prepared compounds were discussed.

LITERATURE CITED

[1] L. Stein, M. Sletzinger, H. Arnold, D. Reinhold, W. Jains, and K. Pfister, J. Am. Chem. Soc. 78, 1514 (1956).

[2] A. Ya. Khorlin, K. I. Lopatina, and N. K. Kochetkov, J. Gen. Chem. 29, 75 (1959).*

[3] J. J. Ritter and P. P. Minieri, J. Am. Chem. Soc. 70, 4045 (1948).

[4] J. J. Ritter and others, J. Am. Chem. Soc. 70, 4048 (1948); 71, 4128, 4130 (1949); 72, 5577 (1950); 73, 4076 (1956).

[5] R. Jacquier, H. Christol, Bull. Soc. Chim. (4), 596, 600 (1957).

[6] A. E. Chichibabin, J. Russ. Chem. Soc. 45, 184 (1913); N. D. Zelinskii and L. Pappe, J. Russ. Chem. Soc. 37, 625 (1905); L. Fawon and M. Barbier, Bull. Soc. Chim. (4), 49, 567 (1931); N. D. Zelinskii, Ber. 34, 2877, 3950 (1901); P. Sabatier and A. Mailhe, C. r. 138, 1322 (1905).

•

---

*Original Russian pagination. See C. B. Translation.

AMINES WITH GANGLIOLYTIC ACTIVITY

II. ALIPHATIC AMINES CONTAINING TERTIARY RADICALS

N. K. Kochetkov, A. Ya. Khorlin, L. A. Vorotnikova, and K. I. Lopatina

Institute of Pharmacology and Chemotherapy of the Academy of Medical Sciences USSR

In the preceding communication [1] we presented data for the synthesis of secondary amines in which one of the radicals is tertiary and is attached to a cyclohexane ring. These compounds, which are simpler analogs of a strong ganglion-blocking agent—3-methylaminoisocamphane (Mecamine)[2]—were less active than Mecamine but nevertheless exhibited marked ganglion-blocking activity. This was a very interesting observation because hardly anything had previously been known about the ganglion-blocking activity of amines.

With the aim of further investigation of the relation between the ganglion-blocking activity and the structure of the amine molecule, we synthesized some even simpler analogs of Mecamine belonging to the aliphatic series and containing a tertiary radical at the nitrogen atom. No information about this type of secondary amine has hitherto appeared in the literature. We synthesized these compounds by the following reactions:

$$\begin{matrix} R_1 \\ R_2 \\ R_3 \end{matrix}\!\!>\!\!C\text{—OH} \xrightarrow{R'CN} \begin{matrix} R_1 \\ R_2 \\ R_3 \end{matrix}\!\!>\!\!C\text{—NHCOR'} \xrightarrow{LiAlH_4} \begin{matrix} R_1 \\ R_2 \\ R_3 \end{matrix}\!\!>\!\!C\text{—NHCH}_2R'$$
$$\text{(I)} \qquad\qquad\qquad \text{(II)} \qquad\qquad\qquad \text{(III)}$$
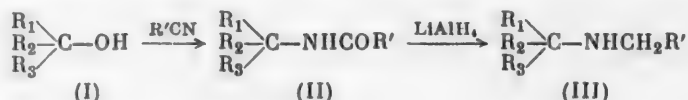
The Ritter reaction [1] was employed for preparation of N-tert-alkylamides (II). Alkylamides (II) were obtained by condensation of readily available tertiary alcohols with acetonitrile or hydrogen cyanide in presence of concentrated sulfuric acid without a solvent (with acetonitrile) or in acetic acid (with hydrogen cyanide) under the conditions that we previously employed. The yields of N-tert-alkylamides (II) depend in large measure on the degree of branching of the chain of the starting alcohol (Table 1) and they generally tend to fall with increasing number of quaternary carbon atoms in the chain. This trend is probably associated with secondary reactions that take place in presence of concentrated sulfuric acid. One possibility is isomerization of the radicals. These secondary reactions can result in a considerable increase in the amount of unwanted impurities. All of the N-tert-alkylamides (II) that we prepared (Table 1) are well-crystallized substances which are easily separated from the reaction mixture. The sole liquid amide [(II), $R_1R_2R_3C = (CH_3)(C_2H_5)(C_3H_7)C$, R' = CH_3] was purified by distillation.

Transition from amides (II) to secondary amines was effected by reduction with lithium aluminum hydride. Maximum yields were obtained by using a 1.5–2-fold excess of the hydride. The secondary amines (III) were immediately converted to the hydrochlorides by saturation of the ethereal solutions of the products with hydrogen chloride. All of them are stable, crystalline substances (Table 2).

All of the prepared amines (III) were subjected to pharmacological tests by D. A. Kharkevich. They exhibited high ganglion-blocking activity: in doses of 2—4 mg/kg they cause blockade of the ganglions for periods of 30 minutes to 2.5 hr.

The most active of the preparations was ethyl-(3-ethyl-3-pentyl)-amine [(III), $R_1 = R_2 = R_3 = R' = C_2H_5$] which approaches Hexonium in activity and toxicity. If one or two of its ethyl radicals are replaced by methyls (compounds 2 and 3 in Table 2), there is a sharp drop in activity. On the other hand, branching of the chain has little influence on the activity. Regarding the influence of a second alkyl radical (R') on the ganglion-blocking activity, the best results are again obtained with ethyl derivatives [(III), R' = C_2H_5]: replacement of ethyl by methyl lowers the activity by a factor of approximately 2.

TABLE 1

Synthesis of Amides R-NH-CO-R'

No.	R	R'	Yield (in %)	Melting point	% N found	Empirical formula	% N calcd.
1	$(CH_3)_3C$		50	97—98°*	—	$C_6H_{13}ON$	—
2	$(CH_3)_2(C_2H_5)C$		51	78—80	10.69, 10.89	$C_7H_{15}ON$	10.84
3	$(CH_3)(C_2H_5)_2C$		50	80—82	9.50, 9.68	$C_8H_{17}ON$	9.77
4	$(C_2H_5)_3C$		55.5	86—87	9.26, 9.25	$C_9H_{19}ON$	8.91
5	$(CH_3)_3C(CH_3)_2C$	CH_3	78.9	109—110	8.83, 8.62	$C_9H_{19}ON$	8.91
6	$(CH_3)_3C(CH_3)(C_2H_5)C$		52	107—109	8.41, 8.45	$C_{10}H_{21}ON$	8.18
7	$(CH_3)_2(n\text{-}C_3H_7)C$		30	57—58	9.80, 9.91	$C_8H_{17}ON$	9.77
8	$(CH_3)_2CH(CH_3)_2C$		30	62—64	9.66, 9.74	$C_8H_{17}ON$	9.77
9	$(CH_3)(C_2H_5)(C_3H_7)C$		32	b. p. 104—106 (5 mm)	9.51, 9.55	$C_9H_{19}ON$	8.91
10	$(CH_3)_2(n\text{-}C_4H_9)C$		93	65—67	9.11, 9.05	$C_9H_{19}ON$	8.91
11	$(CH_3)_3C(CH_3)_2C$	H	32	129—130	10.03, 9.79	$C_8H_{17}ON$	9.77
12	$(C_2H_5)_3C$	H	53	98—100	10.01, 10.06	$C_8H_{17}ON$	9.77

*Literature data [3]: m.p. 97-98°.

TABLE 2

Synthesis of Amides R-NH-CH$_2$-R'·HCl

No.	R	R'	Yield (in%)	Melting point	Found % N	Found % Cl	Empirical formula	% N calcd. N	% N calcd. Cl
1	$(CH_3)_3C$		60	204—205°	—	25.75, 25.47	$C_6H_{16}NCl$	—	25.76
2	$(CH_3)_2(C_2H_5)C$		60	151—153	9.32, 9.42	23.40, 23.20	$C_7H_{18}NCl$	9.23	23.36
3	$(CH_3)(C_2H_5)_2C$		55	160—162	8.60, 8.62	21.30 21.21	$C_8H_{20}NCl$	8.45	21.39
4	$(C_2H_5)_3C$		83.8	178	7.75, 7.79	19.78, 19.73	$C_9H_{22}NCl$	7.79	19.72
5	$(CH_3)_3C(CH_3)_2C$	CH_3	80	256—258	7.94, 7.63	19.74, 19.70	$C_9H_{22}NCl$	7.79	19.72
6	$(CH_3)_3C(CH_3)(C_2H_5)C$		80	209—211	7.45. 7.53	18.32, 18.33	$C_{10}H_{24}NCl$	7.23	18.29
7	$(CH_3)_2(n\text{-}C_3H_7)C$		50	130	8.28, 8.15	21.20, 21.30	$C_8H_{20}NCl$	8.45	21.39
8	$(CH_3)_2CH(CH_3)_2C$		53	174—176	8.22, 8.14	21.28, 21.27	$C_8H_{20}NCl$	8.45	21.39
9	$(CH_3)(C_2H_5)(n\text{-}C_3H_7)C$		63.3	153—156	8.11, 8.08	19.67, 19.77	$C_9H_{22}NCl$	7.79	19.72
10	$(CH_3)_2(n\text{-}C_4H_9)C$		66	153—155	8.14, 8.08	19.61, 19.67	$C_9H_{22}NCl$	7.79	19.72
11	$(CH_3)_3C(CH_3)_2C$	H	63	232—232.5	8.53, 8.57	21.40, 21.38	$C_8H_{20}NCl$	8.45	21.39
12	$(C_2H_5)_3C$	H	50	171—172	8.12, 8.16	21.34, 21.28	$C_8H_{20}NCl$	8.45	21.39

We have thus discovered a new class of ganglion-blocking substances — secondary amines with tertiary radicals. The results of the pharmacological tests of this series point to the desirability of preparation of other compounds of this class, and in particular of the corresponding aliphatic diamines. The latter will be the subject of our next communication.

EXPERIMENTAL

The alcohols (2-methyl-2-butanol, 3-methyl-3-pentanol, 3-ethyl-3-pentanol, 2-methyl-2-pentanol, 2-methyl-2-hexanol, 2,2,3-trimethyl-3-butanol, 2,2,3-trimethyl-3-butanol, 2,2,3-trimethyl-3-pentanol, 2,3-dimethyl-2-butanol, and 3-methyl-3-hexanol) were prepared from the corresponding ketones and alkylmagnesium halides by known methods [4].

N-tert-Alkylacetamides [(II), R' = CH₃]. 0.2 mole of 98% sulfuric acid was stirred in portions at not higher than 40° into a mixture of 0.1 mole of the alcohol and 0.2 mole of acetonitrile. After being kept for 2 days at room temperature, the reaction mass was poured on ice and neutralized with 10% ammonia. The crystals were dried and subjected to distillation at 60—80° (1—2 mm). Data for these N-substituted acetamides appear in Table 1.

N-tert-Alkylformamides [(II, R' = H]. 0.4 mole of 98% sulfuric acid was stirred dropwise at not higher than 10—15° into a suspension of 0.2 mole potassium cyanide in a solution of 0.1 mole of the alcohol (I) and 30 ml glacial acetic acid. The reaction mass was then left for 24 hr at room temperature. The mixture was poured on ice and neutralized with ammonia. The resulting oily layer was extracted with benzene; the extracts were dried with calcium chloride, and the solvent and secondary products were distilled off (toward the end in vacuo until the boiling point of the distillate had reached 80° (20 mm).

The residue (mainly substituted formamide) was purified by recrystallization from a mixture of benzene and ligroine and by subsequent sublimation. Constants and analytical data of the amides are given in Table 1.

Hydrochlorides of amines (III). 0.05 mole of amide (II) was added to a solution of 0.08 mole of lithium aluminum hydride in 50 ml absolute ether, and the reaction mixture was gently boiled for 1—2 hr. Addition was then made (ice cooling) of 100 ml 40% sodium hydroxide solution; the ether layer was separated, the aqueous layer was extracted several times with ether, and the combined ether extracts were dried with solid caustic alkali. After filtration, the dried extract was concentrated to a volume of 15—20 ml. An ethereal solution of hydrogen chloride was then added (with cooling) until the hydrochloride of the amine had been completely brought down. The crystals were filtered, washed on the filter with ether, and recrystallized from absolute acetone. Data for the hydrochlorides of the amines are presented in Table 2.

SUMMARY

1. A new class of gangliolytics—secondary amines containing tertiary radicals— was synthesized by condensation of tertiary alcohols with acetonitrile and subsequent reduction of the amides with lithium aluminum hydride.

2. Data for the relation between the physiological activity and the structure of these amines were discussed.

LITERATURE CITED

[1] N. K. Kochetkov, A. Ya. Khorlin, K. I. Lopatina, and L. A. Vorotnikova, J. Gen. Chem. 29, 3613 (1959).*

[2] A. Ya. Khorlin, K. I Lopatina, and N. K. Kochetkov, J. Gen. Chem. 29, 75 (1959).*

[3] J. J. Ritter and P. Minieri, J. Am. Chem. Soc. 70, 4045 (1948).

[4] A. Dechamps, J. Am. Chem. Soc. 42, 2670 (1920); G. Edgar and others, J. Am. Chem. Soc. 51, 1483 (1929); G. Pariselle, L. Simon, C. r. 173, 86 (1921); L. Henry, C. r. 143, 20 (1906); F. Whitmore, K. Laughlin, J. Am. Chem. Soc. 55, 3732 (1933); L. Clarke, R. Riegel, J. Am. Chem. Soc. 34, 674 (1912); C. H. Lindmer, Monatsh. 32, 419 (1911).

*Original Russian pagination. See C. B. Translation.

INDOLE DERIVATIVES

VI. 6-SUBSTITUTED 1, 2, 3, 4-TETRAHYDRO-γ-CARBOLINES

N. K. Kochetkov, N. F. Kucherova, L. P. Pronina, and M. I. Petruchenko

Institute of Pharmacology and Chemotherapy of the Academy of Medical Sciences USSR

Some derivatives of 1,2,3,4-tetrahydro-γ-carboline possess physiological activity. Among them are preparations with a strong antihistaminic activity [1] whose synthesis has been closely studied [2]. Some derivatives of 1,2,3,4-tetrahydro-γ-carboline containing functional substituents in the 6 position of the carboline ring were also synthesized. A recent report [3] of antimetabolites of serotonin, which are derivatives of 1,2,3,4-tetrahydrocarbazole, renders particularly interesting the synthesis of derivatives of tetrahydro-γ-carboline whose structure still more closely approaches that of serotonin. We also know that substitution at the indole nitrogen atom strongly affects their physiological activity [4].

We have succeeded in synthesizing two types of 6-substituted tetrahydro-γ-carbolines—those not substituted at the indole nitrogen and those containing a n-butyl radical in position 9. The two synthesis were similar in pattern.
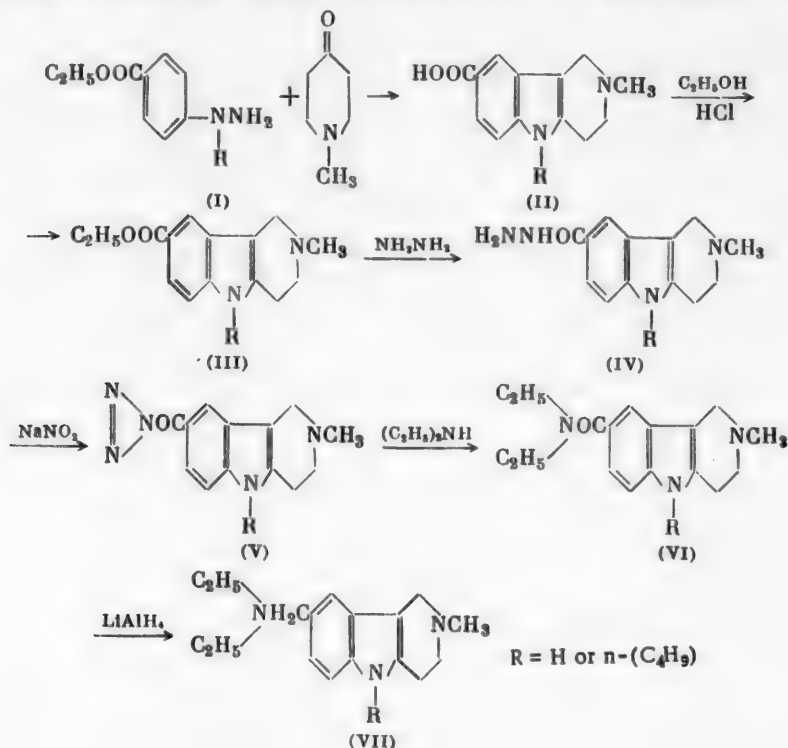
They were based on the Fischer condensation [2]. Condensation of p-carbethoxyphenylhydrazine (I, R = H) and N-(p-carbethoxyphenyl-n-butylhydrazine) (I, R = n-C_4H_9) with N-methyl-γ-piperidone gave 3-methyl-6-

carboxy-1,2,3,4-tetrahydro-γ-carboline (II, R = H) and 3-methyl-6-carboxy-9-butyl-1,2,3,4-tetrahydro-γ-carboline (II, R = C$_4$H$_9$) which served as the main starting substances for further synthesis.

Condensation was effected by heating the components in concentrated hydrochloric acid and gave high yields of tetrahydrocarboline derivatives. At the same time the ester grouping in the original hydrazines was hydrolyzed. All attempts to avoid hydrolysis and to perform this condensation under milder conditions in 7—10% alcoholic hydrochloric acid [2] were unsuccessful because only the hydrochlorides of the original hydrazines were formed. Attempts to cyclize, under the same conditions, previously prepared hydrazones of N-methyl-γ-piperidone similarly led only to hydrolytic breakdown into the original components.

The prepared acids (II, R = H and n-C$_4$H$_9$) were esterified with alcohol in presence of hydrogen chloride, and the resulting esters (III, R = H and n-C$_4$H$_9$) were converted to the corresponding hydrazides (IV) by boiling with alcoholic hydrazine hydrate. In this way a derivative not substituted at the indole nitrogen (V, R = H) was obtained in quantitative yield. Treatment of the hydrazides with sodium nitrite in a weakly acid medium gave the azides (V) (solid crystalline substances without a sharp melting point) which without further purification were brought into reaction with diethylamine to give the diethylamides (VI, R = H and n-C$_4$H$_9$). Reduction of the latter with lithium aluminum hydride in a mixture of ether and tetrahydrofuran led to high yields of 3-methyl-6-diethylaminomethyl-1,2,3,4-tetrahydro-γ-carboline (VII, R = H) and its 9-n-butyl analog (VII, R = n-C$_4$H$_9$).

All of the derivatives of 1,2,3,4-tetrahydro-γ-carboline not containing a substituent at the indole nitrogen atom (R = H) are well-crystallized, easily identifiable substances. Great difficulties were encountered in the preparation of their analogs with an alkyl radical in position 9 (R = n-C$_4$H$_9$), and their yields are lower at all steps of the synthesis. They crystallize with much greater difficulty and two of them—the diethylamide (VI, R = n-C$_4$H$_9$) and the diethylaminomethyl derivative (VII, R = n-C$_4$H$_9$)—are viscous, uncrystallizable oils. They were characterized through the well-crystallized picrate and methiodide.

Considerable interest was also attached to the synthesis of the amidine of 3-methyl-6-carboxy-1,2,3,4-tetrahydro-γ-carboline—the tetrahydrocarabazole analog of which is a most active antagonist of serotonin [3]. We prepared the compound in question by condensation of p-hydrazinobenzamidine with N-methyl-γ-piperidone in concentrated hydrochloric acid.

All of the prepared compounds were handed over for pharmacological investigation, and the results will be reported separately.

EXPERIMENTAL

p-Carbethoxyphenylhydrazine (I, R = H). 11.7 g ethyl p-aminobenzoate, dissolved in 65 ml water and 25 ml conc. HCl, was diazotized at -5° with a solution of 4.5 g NaNO$_2$ in 25 ml water. The solution was filtered and poured into a cold solution of 30 g SnCl$_2$ in 30 ml conc. HCl. The tin complex was filtered off after 15 min, suspended in 50 ml water and treated with 26 ml 40% NaOH. The precipitate was filtered and recrystallized from methanol to give 8.7 g (68%) of substance with m.p. 112—114°.

Found %: N 15.38, 15.42. C$_9$H$_{12}$O$_2$N$_2$. Calculated %: N 15.54.

Hydrochloride: m.p. 220—221°.

Found %: Cl 16.25, 16.11. C$_9$H$_{13}$O$_2$N$_2$Cl. Calculated %: Cl 16.36.

3-Methyl-6-carboxy-1,2,3,4-tetrahydro-γ-carboline (II, R = H). 6.7 g of (I, R = H) and 4.2 g N-methyl-γ-piperidone were boiled for 1.5 hr in 90 ml conc. HCl. The precipitate was filtered and recrystallized from water in presence of carbon. Yield 8.6 g (86%) hydrochloride with m.p. 270—271.5° (decomp.).

Found %: N 10.62, 10.69. C$_{13}$H$_{15}$O$_4$N$_2$Cl. Calculated %: N 10.50.

3-Methyl-6-carbethoxy-1,2,3,4-tetrahydro-γ-carboline (III, R = H). 14 g of the hydrochloride of (II, R = H) was boiled with 280 ml of 2 N alcoholic HCl. The alcohol was driven off in vacuo and the residue recrystallized from aqueous alcohol to give 13 g (85.8%) of hydrochloride with m.p. 244—245° (decomp.).

Found %: N 9.23, 9.45; Cl 12.11, 12.15. C$_{15}$H$_{19}$O$_2$N$_2$Cl. Calculated %: N 9.50; Cl 12.01.

4.2 g of the hydrochloride of the ester was dissolved in water and the aqueous solution made alkaline with aqueous potassium carbonate solution. The precipitate was filtered, washed with water and twice recrystallized

from a mixture of benzene and ligroine. Yield 3.0 g (80%) of 3-methyl-6-carbethoxy-1,2,3,4-tetrahydro-γ-carboline with m.p. 145—146°.

Found %: N 11.09, 10.97. $C_{15}H_{18}O_2N_2$. Calculated %: N 10.84.

Methiodide. 1.2 g (III, R = H) was dissolved in 200 ml absolute ether, 4.5 g CH_3I was added and the mixture stood at room temperature for 48 hr. The precipitate was filtered off and recrystallized from water to give 1.6 g of methiodide with m.p. 225—226°.

Found %: N 6.69, 6.75, I 31.83, 31.93 $C_{16}H_{21}O_2N_2I$. Calculated %: N 6.99; I 31.71.

3-Methyl-6-carboxyhydrazide-1,2,3,4-tetrahydro-γ-carboline (IV, R = H). 4.8 g of (III, R = H) was boiled in 40 ml anhydrous alcohol with 18 ml 98% hydrazine hydrate for 18 hr. The precipitate was filtered, the alcoholic solution was evaporated in vacuo, and the residue was run into water. The resulting precipitate was filtered and the combined precipitates were recrystallized from anhydrous alcohol to give 3.9 g (84.7%) with m.p. 243—245°.

Found %: N 22.72, 22.84. $C_{13}H_{16}ON_4$. Calculated %: N 22.93.

3-Methyl-6-carboxydiethylamido-1,2,3,4-tetrahydro-γ-carboline (VI, R = H). 8 g of (IV, R = H) was dissolved in 1 liter water with 52 ml conc. HCl. The reaction mixture was cooled to 0° and 2.6 g $NaNO_2$ in 35 ml water was added. The resulting suspension of the hydrochloride of the azide (V, R = H) was held in the cold for 2 hr. It was thereupon made alkaline with saturated potassium carbonate solution; the precipitate was filtered, washed with water, and dried in vacuo to give 8.8 g (91%) of product without a definite melting point. It decomposed on heating.

8.8 g of (V, R = H) was boiled for 1 hr with 35 ml diethylamine. The excess of diethylamine was distilled off and the residue was recrystallized from dioxane with addition of carbon. There was obtained 5.8 g (51.8%) of (VI, R = H) with m.p. 137.5—138°.

Found %: C 71.70, 71.78; H 8.16, 8.22. $C_{17}H_{23}ON_3$. Calculated %: C 71.54; H 8.12.

3-Methyl-6-diethylaminomethyl-1,2,3,4-tetrahydro-γ-carboline (VII, R = H). 2.1 g of carboxyamide (VI, R = H) in 25 ml tetrahydrofuran was brought into an ethereal solution of $LiAlH_4$ (from 7.2 g $AlBr_3$ and 0.88 g LiH in 30 ml ether), and the reaction mass was stirred 20 hr at room temperature. The excess of $LiAlH_4$ was decomposed with water and the reaction mixture was made alkaline with conc. NaOH. The ether—tetrahydrofuran extract was separated. The aqueous layer was twice extracted with ether, and the combined extracts were dried over ignited potassium carbonate. The solvents were distilled off. The residue crystallized. It was recrystallized from ligroine. Yield 1.5 g of (VII, R = H) (77.7%) with m.p. 118—120°.

Found %: C 75.37, 75.32; H 9.13, 9.06; N 15.01, 15.15. $C_{17}H_{25}N_3$. Calculated %: C 75.23; H 9.27; N 15.43.

Dihydrochloride of 3-methyl-6-carboxyamidino-1,2,3,4-tetrahydro-γ-carboline. 2.4 g p-hydrazinobenzamidine [3] and 1.5 g N-methyl-γ-piperidone was boiled 1.5 hr with 30 ml conc. HCl. A precipitate came down on cooling and was filtered. Yield 1.5 g (84.3%). M.p. 305—306° (decomp.) after 3 recrystallizations from 85% isopropyl alcohol.

Found %: C 51.20; H 6.4; N 18.64, 18.72. $C_{13}H_{18}N_4Cl_2$. Calculated %: C 51.83; H 6.02; N 18.60.

n-Butyl-(p-carbethoxyphenyl)-nitrosoamine. 37 g of n-butyl-p-carbethoxyaminobenzoic acid [5] was dissolved in 370 ml alcohol containing 19 ml conc. H_2SO_4. The reaction mixture was cooled to -5° and a solution of 11.5 g $NaNO_2$ in 1.5 liter water was added dropwise. The ethereal extract was dried with anhydrous Na_2SO_4 and the ether was distilled off. Yield 35 g (83%) of a yellow-red oil which was reduced without purification.

N-(p-Carbethoxyphenyl)-N-n-butylhydrazine. 22 g of n-butyl-p-carbethoxyphenylnitrosoamine was dissolved in 100 ml alcohol. Addition was then made of 60 g zinc dust and 25 ml acetic acid at such a speed that the temperature did not exceed 40°. The reaction mixture was then stirred 1 hr, the excess of zinc was filtered off, and the filtrate was evaporated to $\frac{1}{4}$ of its original volume. To the residue was added an equal volume of water and the solution was made strongly alkaline with 40% NaOH. It was then extracted 3 times with ether. The ether extract was dried with Na_2SO_4 and a stream of dry hydrogen chloride was passed through it. There was obtained 11 g (46.2%) of the hydrochloride. Part of the product was quickly recrystallized from conc. HCl; m.p. 160—163°.

Found %: N 10.21, 10.09; Cl 12.66, 12.87. $C_{13}H_{21}O_2N_2Cl$. Calculated %: N 10.27; Cl 12.99.

Hydrochloride of 3-methyl-6-carboxy-9-n-butyl-1,2,3,4-tetrahydro-γ-carboline (II, R = n-C_4H_9). 0.5 g of hydrochloride of N-(p-carbethoxyphenyl)-N· n-butylhydrazine and 0.25 g N-methyl-γ-piperidone were boiled for 1.5 hr with 7 ml conc. HCl. The reaction mass was evaporated to dryness in vacuo. To the residue was added a few ml of warm anhydrous alcohol and the solution was filtered. Trituration for a short time resulted in deposition of white crystals which were filtered. Yield 0.4 g (54%). M.p. 120−122° (decomp.) after recrystallization from anhydrous alcohol.

Found %: N 8.38; 8.64; Cl 10.76, 10.45. $C_{17}H_{23}O_2N_2Cl$. Calculated %: N 8.67; Cl 10.98.

Hydrochloride of 3-methyl-6-carbethoxy-9-n-butyl-1,2,3,4-tetrahydro-γ-carboline (III, R = n-C_4H_9). 2 g of the hydrochloride of (II, R = n-C_4H_9) was boiled 12 hr with 50 ml of 20% solution of hydrochloric acid in anhydrous alcohol. The alcohol was distilled off in vacuo and the residue was recrystallized from a mixture of anhydrous alcohol and ether. There was obtained 1.5 g (71.4%). M p. 210−211.5° after two recrystallization from a mixture of anhydrous alcohol and ether.

Found %: C 65.07, 65.27; H 8.05, 7.96; N 7.98, 8.07; Cl 9.75, 9.67. $C_{19}H_{27}O_2N_2Cl$. Calculated %: C 65.03; H 7.72; N 7.98; Cl 10.10.

3-Methyl-6-carboxyhydrazido-9-n-butyl-1,2,3,4-tetrahydro-γ-carboline (IV, R = n-C_4H_9). 8.5 g of the hydrochloride of (III, R = n-C_4H_9) was dissolved in a small quantity of water and potassium carbonate solution was added until the reaction was alkaline. An oil separated out and was extracted with ether. The ethereal extract was dried with anhydrous Na_2SO_4, and the ether was distilled off in vacuo to leave 7.1 g of non-crystallizing, light-yellow oil; this was dissolved in 57 ml anhydrous alcohol, 25 ml hydrazine hydrate was added, and the reaction mass was refluxed for 18 hr. The alcohol was distilled off in vacuo and the residue was poured into a ten-fold volume of water. An oil separated. The water was decanted off and to the residue was added 2−3 ml benzene. The reaction mass then crystallized completely. Yield 6.7 g (89.3%). Two recrystallizations from benzene gave thin, colorless needles with m.p. 144−145°.

Found %: N 18.37, 18.44. $C_{17}H_{24}ON_4$. Calculated %: N 18.65.

3-Methyl-6-carboxydiethylamido-9-n-butyl-1,2,3,4-tetrahydro-γ-carboline (VI, R = n-C_4H_9). 1.5 g of (IV, R = n-C_4H_9) was dissolved in 220 ml water containing 9.8 ml conc. HCl. The reaction mass was cooled to 0°, 0.4 g of $NaNO_2$ in 5 ml of water was stirred in, and the mass was held at the same temperature for another 1.5 hr before being neutralized with potassium carbonate solution. The azide (V, R = n-C_4H_9) separated out and was filtered, washed with water, and dried in vacuo. The azide is stable at room temperature but does not possess a definite melting point. Weight 1.1 g (69%).

0.5 g of the azide was heated for 15 min with 3 ml diethylamine and kept for 1 hr at room temperature; excess of diethylamine was removed in vacuo. A light-yellow oil was obtained which did not crystallize from various solvents. It was dried in vacuo. Yield 0.5 g (90%).

Picrate: m.p. 190−192° (decomp.) after recrystallization from aqueous alcohol. Yellow needles.

Found %: C 57.10, 56.99; H 6.27, 6.22; N 14.27, 14.41. $C_{27}H_{34}O_8N_6$. Calculated %: C 56.77; H 6.00; N 14.27.

3-Methyl-6-diethylaminomethyl-9-n-butyl-1,2,3,4-tetrahydro-γ-carboline (VII, R = n-C_4H_9). 5.5 g of carboxyamide (VI, R = n-C_4H_9) in 50 ml tetrahydrofuran was put into an ethereal solution of $LiAlH_4$ (from 19 g $AlBr_3$ and 2.4 g LiH in 100 ml ether). The reaction mixture was stirred for 24 hr at room temperature. Treatment on the lines of that for 3-methyl-6-diethylaminomethyl-1,2,3,4-tetrahydro-γ-carboline (VI, R = H) gave 5 g (96%) of a light-yellow, noncrystallizing mass.

Dimethiodide. 2.5 g of the oil was dissolved in 100 ml ether; 6 g methyl iodide was added, and the mass was stood at room temperature for 24 hr. The precipitate was filtered and twice recrystallized from anhydrous alcohol. Yield 9 g (93.7%) with m.p. 178−180.5°.

Found %: C 45.58; H 6.54; I 41.78, 41.56; N 6.53, 6.61. $C_{23}H_{39}N_3I_2$. Calculated %: C 45.16; H 6.43; N 6.87; I 41.51.

SUMMARY

The synthesis is described of a series of derivatives of 3-methyl-1,2,3,4-tetrahydro-γ-carboline and of 3-methyl-9-n-butyl-1,2,3,4-tetrahydro-γ-carboline containing functional substituents in position 9.

LITERATURE CITED

[1] U. Hörlein, Ber. <u>87</u>, 463 (1954).

[2] N. F. Kucherova and N. K. Kochetkov, J. Gen. Chem. <u>26</u>, 3149 (1956).*

[3] E. Show and D. W. Wolley, J. Am. Chem. Soc. <u>79</u>, 3560 (1957).

[4] D. A. Kharkevich, Clinical Medicine, No. 5 (1957); Pharmacology and Toxicology, No. 6 (1957).*

[5] H. Shapiro, J. Soc. Chem. Ind. <u>64</u>. 177 (1945).

---

* Original Russian pagination. See C. B. Translation.

THE DISSOCIATION OF MALACHITE GREEN BASE

K. Shekhter, A. V. Savitskii, and I. I. Moiseev

Institute of Fine Chemical Technology

The dissociation of triarylcarbinols is of interest as a reaction that yields a stable carbonium ion. Several studies have been made of reactions of this type [1, 2], but in no instance have the equilibrium values of ΔH and ΔS been determined.

In the present work a spectrophotometric study is made of the dissociation of Malachite Green in aqueous solution containing about 3% of dioxane at 15, 25, and 35° in presence of a phosphate buffer (pH from 5.29 to 8.04).

If the dissociation equilibrium is not complicated by secondary processes and if the optical density of the solution is proportional to the concentration of the cation of the dye, then the following equation expresses the dependence of the optical density D on the pH and the initial carbinol concentration $[ROH]_0$:

$$D = \frac{\varepsilon \cdot d}{1 + K_h/[H^+]}\,[ROH]_0,$$

where ε is the extinction coefficient of the carbonium ion, $\underline{d}$ is the layer thickness, and K_h is the hydrolysis constant.

It follows from equation (1) that when the pH is constant the value of D is proportional to that of $[ROH]_0$. Results of experiments at pH 7.73 are plotted in the diagram.

In order to find the hydrolysis constant we must know the value of the extinction coefficient ε. We calculated the following values of ε from the optical density of the solution at pH 5.29 (when the carbinol is completely dissociated): $7.70 \pm 0.26 \cdot 10^4$ (λ 620 mμ) and $2.17 \pm 0.10 \times 10^4$ liter·mole^{-1}·cm^{-1} (λ 562 mμ).

The dissociation constants K of the base were obtained from the values of K_r calculated with the help of equation (1). Results of the experiments are shown in the table, together with the values of ΔH and ΔS found by the method of least squares from the temperature dependence of log K.

In the experiments carried out with $\mu = 0.01$ g-ion × liter^{-1}, the error in the values of -log K -is greater than in the experiments with $\mu = 0.05$ g-ion × liter^{-1}. This is probably because in the calculations for the first series of experiments we used tabulated values of pH [3] whereas for the second series we used the pH values obtained potentiometrically. Later it was found desirable to consider only the values $\Delta H = 10.6$ kcal × mole^{-1} and $\Delta S = 4.18$ esu. For our selected buffer concentrations, we can neglect the values of $\Delta H\mu$ and $\Delta S\mu$ which are associated with ions of foreign electrolytes.

It should be noted that in our case the ΔS of the reaction is considerably larger than in the case of dissociation of protonic acids ($\Delta S \approx -22 \pm 5$ esu [4]). This difference is consistent with the hypothesis that the cation of a dye is very much more weakly hydrated than a hydrogen ion.
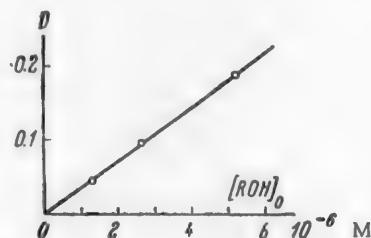
Optical density of the solution as as function of the initial concentration of the carbinol for $\mu = 0.05$ g-ion × liter^{-1} pH 7.73 and t = 35°.

μ (g-ion · liter^{-1})	Temp.	pH range	-log K	Δ_H in $\frac{kcal}{mole}$	Δ_S(esu)	-log K by least squares	No. of expt.
0.01	15 25 35	5.29—8.04	7.19 ± 0.10 6.84 ± 0.16 6.62 ± 0.13	11.7	8.12	7.19 6.89 6.61	5 16 6
0.05	15 25 35	5.29—7.73	7.15 ± 0.03 6.92 ± 0.07 6.67 ± 0.05	10.6	4.18	7.16 6.89 6.63	4 9 6

On the basis of the literature data [2] and our own data, we can calculate the activation parameters for the dissociation of the carbinol to ions: $\Delta H^{\#}$ = 25 kcal mole $^{-1}$, $\Delta S^{\#}$ = 6.2 esu. The negative entropy of activation indicates that in the transition state the carbinol molecule is strongly polarized (or constitutes an ionic pair) and solvation effects play an important part.

Hydrolysis of triphenylmethyl acetate in 70% aqueous dioxane and methanol with rupture of the alkyl-oxygen bond is associated with an entropy of activation of -3.7 and -7.5 esu respectively [5]. In this reaction it is possible that the activated complex is likewise the solvated polarized molecule or an ionic pair [6].

EXPERIMENTAL

4,4'-Tetramethyldiaminotriphenylcarbinol, * m.p. 120—122° (from toluene).

For measurement of the optical density, solutions of 4,4'-tetramethyldiaminotriphenylcarbinol were mixed with a certain quantity of buffer mixture such that, in the final solution, the concentration of dioxane was 2.9%. The solution was thermostatted in a flask whose walls were coated with synthetic paraffin wax. After equilibrium had been established (8 hr at 25°), the solution was transferred to a cell (thermostatted to within ± 0.1°) and the spectral characteristics were recorded on an SF-2M instrument. The initial concentration of the carbinol was usually 5.23×10^{-6} mole $\times$ liter^{-1}.

Measurements of pH were carried out potentiometrically with calomel and hydrogen electrodes using a high-ohmic potentiometer of the PPTV-1 type. The null instrument was a mirror galvanometer with a sensitivity of 7.7×10^{-10} amp/mm.

SUMMARY

1. Dissociation constants of Malachite Green base were determined at 15, 25, and 35°. The values ΔH = 10.6 kcal mole $^{-1}$ and ΔS = 4.18 esu were obtained.

2. A theory of structure of the activated complex during dissociation of the carbinol is advanced.

LITERATURE CITED

[1] R. J. Goldacre, J. N. Phillips, J. Chem. Soc. 1949, 1724; P. Rumpf, M. Gillois, Bull. Soc. chim 1954, 118; O. F. Ginzburg, J. Gen. Chem. 23, 1504 (1953);** O. F. Ginzburg and N. S. Mel'nikova, J. Gen. Chem. 25, 1156 (1955);** O. F. Ginzburg and P. M. Zavlin, J. Gen. Chem. 27, 678 (1957).**

[2] J. C. Turgeon, V. K. La Mer, J. Am. Chem. Soc. 72, 5988 (1952).

[3] Handbook of Chemistry, Vol. III [in Russian] (State Chem. Press, 1952), p. 525.

[4] K. S. Pitzer, J. Am. Chem. Soc. 59, 2365 (1937).

[5] C. A. Bunton, A. E. Comyns, J. Graham, J. R. Quayle, J. Chem. Soc. 1955, 3817.

[6] Ya. K. Syrkin and I. I. Moiseev, Prog. Chem. 27, 717 (1958).

* Kindly placed at our disposal by O. F. Ginzburg.

** Original Russian pagination. See C. B. Translation.

HYDROGENATION OF FURAN COMPOUNDS OVER NICKEL CATALYSTS

N. I. Shuikin and I. F. Bel'skii

Institute of Organic Chemistry of the Academy of Sciences USSR

The results of our preceding investigations [1] showed that catalysts containing metals of group VIII of the Periodic System and deposited on active carbon can be arranged in two classes on the basis of their action on the furan ring under the conditions of vapor phase hydrogenation. Platinum, ruthenium, rhodium, osmium, and iridium are substantially inactive or only weakly active as catalysts for the hydrogenation of the furan ring. At temperatures of about 150° these catalysts selectively catalyze the hydrogenation of the double bond in the side chain of α-alkenyl furans without acting on the furan ring; at higher temperatures (250–300°) they catalyze the hydrogenolysis of the furan ring exclusively at the C—O bond remote from the side alkyl group (the 1- 5 C—O bond):

$$\underset{1}{\overset{4\quad3}{\underset{5\quad 2}{\boxed{}}}}\text{—R} \xrightarrow[250-300°]{H_2} CH_3CH_2CH_2-\underset{\underset{O}{\|}}{C}-R \quad (I)$$
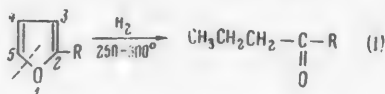
Under specific conditions these catalysts can therefore be described as furan ring hydrogenolysis catalysts.

Palladium on carbon behaves entirely differently. Over a fairly wide temperature range (140–275°) it specifically catalyzes the hydrogenation of double bonds in the furan ring [2]. The yield of tetrahydrofurans is substantially quantitative at lower temperatures but falls to about 80% at 275°. The properties of nickel catalysts are profoundly influenced by the nature of the support. Nickel on zinc oxide, for example, behaves entirely like catalysts of the platinum group in respect of the vapor phase hydrogenation of the furan ring and of the double bond in the side chain of α-alkenylfurans [3]. On the other hand skeletal nickel—aluminum catalyst, like palladium on carbon, at 120 – 150° smoothly catalyzes the hydrogenation of the furan ring [4], while at higher temperatures it brings about (apart from fission of the furan ring at the 1- 5 C—O bond) "conjugated hydrogenolysis" which results in the formation from a molecule of α-alkylfuran of a molecule of aliphatic alcohol or ketone and a molecule of hydrocarbon [5] according to the scheme:

$$\underset{1}{\overset{4\quad3}{\underset{5\quad 2}{\boxed{}}}}\text{R} \xrightarrow[Ni-Al]{H_2} \begin{array}{l} \xrightarrow{\text{Rupture of the 1-5 and 4-5 bonds}} CH_3CH_2-\underset{\underset{O}{\|}}{C}-R + C_nH_{2n+2} \\[2em] \xrightarrow{\text{Rupture of the 1-5 and 3-4 bonds}} CH_3-\underset{\underset{O}{\|}}{C}-R + C_nH_{2n+2} \end{array} \quad (II)$$
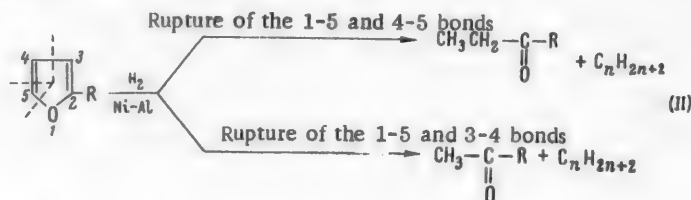
More thorough investigation of the properties of nickel catalysts in dependence on the nature of the support is called for, in view of our observations that only skeletal nickel—aluminum catalyst is capable of bringing about conjugated hydrogenolysis of the furan ring and that nickel on zinc oxide is entirely devoid of this property. Two problems stand out in this connection:

1. Apart from zinc oxide, which oxides, when used as supports, endow nickel with the properties of catalysts of the platinum group?

2. Does the ability of skeletal nickel—aluminum to catalyze the conjugated hydrogenolysis of the furan ring depend on the presence of aluminum? The same question can be expressed more generally: To what extent are

the properties of skeletal nickel—metal catalysts governed by the nature of the second, "inactive" component?

With the objective of answering the first question, we investigated in the present work the catalytic properties of nickel, deposited on the oxides of beryllium, cadmium,and barium, in the hydrogenation of sylvan and α-propenylfuran. The reaction was run under identical conditions with all of the three catalysts: flow system, normal pressure, temperatures of 175 and 300°. Nickel on barium oxide was found to be inactive, but nickel on beryllium oxide and cadmium oxide exhibited properties similar to those of nickel on zinc oxide, although hydrogenation of the side chain double bond and hydrogenolysis of the furan ring went less smoothly over the new catalysts. At 175° sylvan remained unchanged after passage in admixture with hydrogen over nickel on cadmium oxide or beryllium oxide, but α-propenylfuran was hydrogenated to α-propylfuran in yields of about 90%
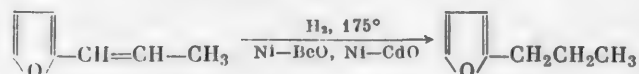
Hydrogenation of sylvan over nickel on beryllium oxide or cadmium oxide at 300° led, as in the case of nickel on zinc oxide, to hydrogenolysis of the furan ring at the 1 - 5 C—O bond with formation of methyl propyl ketone.
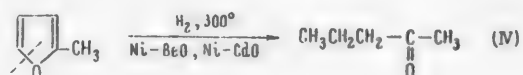
In presence of nickel on zinc oxide, hydrogenolysis of the furan ring takes place without formation of any secondary reactions; by contrast, over nickel on beryllium or cadmium oxide,methyl propyl ketone is formed in a yield of 70—85%; the residue is a substance with a high boiling point. It should also be noted that nickel on beryllium oxide or cadmium oxide is very much less active than nickel on zinc oxide.

The answer to the second question was given by an investigation of the properties of skeletal nickel—zinc catalyst prepared by partial removal of zinc from a nickel—zinc alloy. Comparison of the properties of skeletal nickel—zinc and nickel—aluminum catalysts in the hydrogenation of furan compounds shows that the nature of the second component is responsible for the great qualitative difference between these catalysts. In the first place, skeletal nickel—zinc catalyst differs from skeletal nickel—aluminum catalyst in showing extremely low activity in the hydrogenation of furan ring double bonds. At 150° sylvan slowly reacts with hydrogen over skeletal nickel—zinc catalyst to form tetrahydrosylvan (10—15%), 2-pentanol (70%) and 2-pentanone (15—20%). At 300° sylvan is substantially quantitatively converted into methyl propyl ketone. Consequently, even at low temperature,skeletal nickel—zinc catalyst predominantly catalyzes the hydrogenolysis of the furan ring and in its properties it therefore more closely resembles nickel on zinc oxide than skeletal nickel—aluminum.

Still more striking is the difference between skeletal nickel—aluminum and nickel—zinc: the former promotes conjugated hydrogenolysis of the furan ring (reaction II) and this property is entirely lacking from the latter; in this respect the latter behaves qualitatively and quantitatively exactly like nickel on zinc oxide in causing fission of the furan ring exclusively at the 1 - 5 C—O bond (reaction I). The great similarity of skeletal nickel—zinc and nickel on zinc oxide is equally manifested in the hydrogenation of α-propenylfuran, this reaction (at 150—160°) leading to α-propylfuran (90%) and 4-heptanone (10%); similarly at 300° ethylfurylcarbinol is reduced to α-propylfuran, but the latter undergoes hydrogenolysis to 4-heptanone.
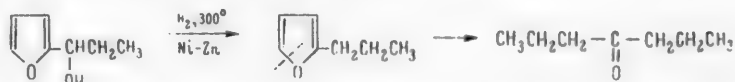
To a certain degree the above results indicate that the active centers of skeletal nickel—zinc catalyst and nickel on zinc oxide are identical in character and contain only atoms of nickel and zinc.

EXPERIMENTAL

Starting substances. Pure sylvan, isolated from the commercial product by distillation in a column over sodium, had b.p. 63—64° (750 mm), d_4^{20} 0.9120, n_D^{20} 1.4321. Ethylfurylcarbinol and α-propenylfuran were synthesized by the reactions:

(I)

$$\text{furyl-}C\overset{O}{\underset{H}{\diagdown}} \xrightarrow{C_2H_5MgBr} \text{furyl-}CHCH_2CH_3 \ (OH) \xrightarrow[350-400°]{ZrO_2} \text{furyl-}CH=CH-CH_3$$
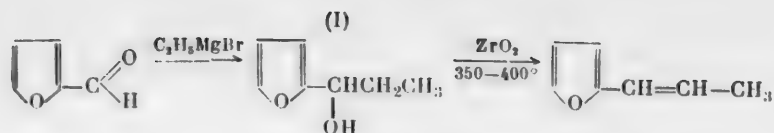
The ethylfurylcarbinol was distilled: b.p. 73—75° (8 mm), d_4^{20} 1.0492, n_D^{20} 1.4786. α-Propenylfuran, isolated from the products of dehydration by fractional distillation in a column, had b.p. 132—133° (752 mm), d_4^{20} 0.9457, n_D^{20} 1.5098.

Catalysts. Nickel on beryllium oxide and on barium oxide was prepared by impregnation of the oxide powders with the calculated quantity of concentrated nickel nitrate solution. After drying in an electrically heated cupboard at 120—130°, the nickel nitrate-impregnated oxides were shaped into cylinders and place in a reaction tube of quartz. The nickel nitrate was decomposed at 300—400° in the course of 10—15 hr in a continuous air stream. The catalysts were thereupon reduced with hydrogen for 10 hr while the temperature was steadily raised from 200 to 350°

Nickel on cadmium oxide was prepared by precipitation of nickel and cadmium hydroxides with potassium hydroxide from their dissolved nitrates. The precipitate was washed with water until nitrate ions had disappeared (test with diphenylamine), filtered, dried at 120—130°, shaped into small cylinders, and transferred to the reaction tube. Reduction with hydrogen was performed as in the preceding cases.

All of the catalysts contained about 30% nickel.

Skeletal nickel—zinc catalyst was prepared by treatment of granules of nickel—zinc alloy (30% nickel) with concentrated sodium hydroxide solution with strong heating. Zinc removal from the alloy by leaching was very much more difficult than removal of aluminum from nickel—aluminum alloy, and it necessitated longer and more vigorous heating. After the caustic alkali treatment, the catalyst was washed free of alkali with water (test with phenolphthalein) and was charged in the moist condition into the reaction tube. We made use of catalysts from which about 20—25% of the zinc content had been removed from nickel—zinc alloy.

Experimental conditions. Sylvan, α-propenylfuran and ethylfurylcarbinol were hydrogenated in a flow system at normal hydrogen pressure. The reactor was a quartz tube into which the substance was charged from an automatic buret at a space velocity of 0.1 hr^{-1}. 50 ml catalyst was put into the tube. The amounts of sylvan, α-propenylfuran and ethylfurylcarbinol in each experiment were 50, 25, and 65 g respectively. The catalyzates were dried with calcium chloride and fractionally distilled in a 40-plate column. The table shows the properties of the products of hydrogenation and hydrogenolysis of sylvan, α-propenylfuran and ethylfurylcarbinol.

Products of hydrogenation	b. p. (pressure in mm)	d_4^{20}	n_D^{20}	M. p. of semicarbazone
2-Pentanone	101—102 (748)	0.8081	1.3912	110
α-n-Propylfuran .	114—115 (745)	0.8876	1.4395	
4-Heptanone	142.5—143 (750)	0.8176	1.4085	132

SUMMARY

1. Nickel deposited on beryllium oxide or cadmium oxide resembles nickel on zinc oxide in being incapable of catalyzing the vapor phase hydrogenation at normal pressure of the furan ring.

Over these catalysts at 175° only hydrogenation of the double bond of the side chain takes place, while at 300° the ring suffers hydrogenolysis at the C—O bond remote from the side alkyl group.

2. It was found that the properties of skeletal nickel catalysts are strongly dependent on the nature of the second component. Skeletal nickel—zinc catalyst differs from skeletal nickel—aluminum catalyst in having extremely low activity in the hydrogenation of double bonds of the furan ring in the vapor phase at normal pressure. Like nickel on zinc oxide, skeletal nickel—zinc catalyst does not catalyze conjugated hydrogenolysis and it cleaves the furan ring exclusively at the 1- 5 C—O bond.

LITERATURE CITED

[1] N. I. Shuikin, I. F. Bel'skii, and Kh. M. Minachev, J. Gen. Chem. <u>29</u>, 2969 (1959). *

[2] N. I. Shuikin, V. L. Nikiforov, and P. A. Stolyarova, J. Gen. Chem. <u>7</u>, 1501 (1937); N. I. Shuikin and I. F. Bel'skii, Proc. Acad. Sci. USSR <u>115,</u> 330 (1957). *

[3] N. I. Shuikin and I. F. Bel'skii, J. Gen. Chem. <u>29</u>, 442 (1959). *

[4] N. I. Shuikin and V. I. Bunina, J. Gen. Chem. <u>8</u>, 669 (1938).

[5] N. I. Shuikin and I. F. Bel'skii, Bull. Acad. Sci. USSR, Div. Chem. Sci. 309 (1958). *

---

*Original Russian pagination. See C. B. Translation.

SYNTHESIS AND SOME REACTIONS OF SULFIDES OF THE THIOPHENE SERIES

II. THE RELATIVE MOBILITY OF THE HYDROGEN ATOMS OF SOME ALKYLTHIENYL SULFIDES UNDER CONDITIONS OF METALATION WITH n-BUTYLLITHIUM

Ya. L. Gol'dfarb, M. A. Kalik, and M. L. Kirmalova

Institute of Organic Chemistry of the Academy of Sciences USSR

Metalation of thiophene and its substituted derivatives is a convenient method of preparation of intermediates for the synthesis of diverse derivatives containing the thiophene nucleus (compare, for example, [1]). Very little published information has appeared about the influence of the nature of the substituents in the ring on the course of the reaction. A theory has been advanced which involves primary coordination of the metalating agent [2] (at the expense of the unshared electron pair of the heteroatom). Consideration has also been given to the factor determining the site of subsequent attack and therefore limiting or excluding the influence of substituents [3]. These speculations have proved far from adequate for explaining a number of features observed during metalation. For example, whereas anisole is metalated by n-butyllithium in the ortho position to the methoxyl, methylphenyl sulfide [4,5] and phenylbenzyl sulfide [6] give exclusively products substituted in the side chain. Again, when n-butyllithium acts on ethyl-2-thienyl sulfide [7] the ring hydrogen is substituted, as shown by one of us, G. I. Gorushkina and B. P. Fedorov [7], although it is difficult on the basis of existing knowledge to attribute to the thiophene sulfur a "stronger" coordinating effect than sulfide sulfur, the participation of which in the process might lead to a product metalated in the side chain. Another possibility, however, is that a secondary product is formed at the start and subsequently metalates another molecule of sulfide in the ring.

In the light of the foregoing facts and the data of Sicé [8], who showed that 2-methoxythiophene is metalated in the α position, interest is attached to a study of the action of butyllithium on methyl-2-thienyl sulfide (II) and methyl (5-methyl-2-thienyl) sulfide (III).
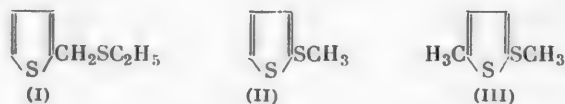
In these cases the thiophene sulfur and the side chain sulfur differ less in potential ability to add on a molecule of n-butyllithium than do the sulfur atoms in ethyl-2-thienyl sulfide, since the former resemble one another in the character of their behavior towards the π-electron system of the nucleus [for example (IV) and (V)], whereas the latter are markedly different from one another.
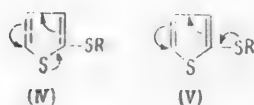
The results of our experiments on the metalation of sulfides of types (II) and (III) can be summed up as follows. Methyl-2-thienyl sulfide (II) easily reacts with n-butyllithium to give the lithium derivative (VI) in good yield; the latter has the metal in the thiophene ring. Methylphenyl sulfide behaves differently in this reaction. The structure (VI) was verified by its transformation into 5-methyl-mercapto-2-thiophenecarboxylic acid (VII), which had previously been obtained by oxidation of 3-methylmercapto-thiophenealdehyde (VIII) [9].

OHC⟨S⟩SCH₃ → HOOC⟨S⟩SCH₃ ←CO₂— Li⟨S⟩SCH₃ —S/CH₃I→ H₃CS⟨S⟩SCH₃

(VIII)　　　　　(VII)　　　　　　(VI)　　　　　　(IX)

In similar fashion 2-thienyl sulfide gave 5-ethylmercapto-2-thiophenecarboxylic acid in 76% yield.

Reaction of (VI) with sulfur and methyl iodide leads to 2,5-bis-(methylmercapto) thiophene (IX), which we described in the preceding paper [10]. The facility with which methyl-2-thienyl sulfide is metalated is undoubtedly bound up with the activating influence of the alkylmercapto group. This explanation is supported by an experiment on the metalation of an equimolar mixture of thiophene and methyl-2-thienyl sulfide with a deficiency of n-butyllithium. Carboxylation of the reaction product gave acid (VII) in 70% yield; the 2-thiophenecarboxylic acid could not be detected. Since nucleophilic properties are attributed to lithiumalkyls in view of their metalating ability [2], such an influence of the SR group is difficult to explain. We must evidently accept Gilman's view that this interpretation of the metalation provess is not the only possible one.

Metalation of methyl (5-methyl-2-thienyl) sulfide (III) and of ethyl (5-ethyl-2-thienyl) sulfide with n-butyllithium goes much more sluggishly. In the case of (III), marked darkening of the reaction mass is observed within a short time after mixing of the reactants; suitable working-up led to isolation of acid (X) in a yield of only about 3%; about 85% of the original sulfide was recovered. The yield of acid can be raised to 27% by short-period heating of the mixture, but this procedure leads to loss of sulfide.

H₃C⟨S⟩SCH₃(Li) → H₃C⟨S⟩SCH₃(COOH) ← H₃C⟨S⟩SCH₃(COCH₃)

　　　　　　　　　(X)　　　　　　　　　　　(XI)
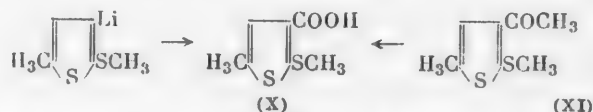
On the basis of these experiments we can say that the β hydrogen atoms of the thiophene ring are replaced by metal with very much greater difficulty than the α atoms are replaced. Moreover, attempts in our laboratory to metalate 2,5-dimethylthiophene were unsuccessful. It therefore becomes obvious that the formation of acid (X) can also be associated with an inductive effect of the alkylmercapto group. The structure of this acid was confirmed by its synthesis from 2-methylmercapto-5-methyl-3-acetothienone (XI) [10]. Its isomer (XII), which might have been formed by metalation of (III), was synthesized by us by condensation of lithium 5-methyl-2-thienylmercaptide (XIII) with ethyl bromoacetate followed by hydrolysis of ester (XIV), but acid (XII) is easily distinguished from acid (X) by its melting point.

H₃C⟨S⟩ → H₃C⟨S⟩SLi → H₃C⟨S⟩SCH₂COOC₂H₅ → H₃C⟨S⟩SCH₂COOH

　　　　　(XIII)　　　　　　　(XIV)　　　　　　　　　(XII)
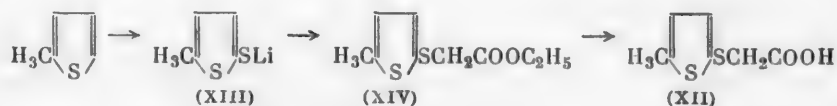
Due to the small amount of experimental material, it is not yet possible to generalize the conclusions relating to the direction of the metalation reactions of sulfides of the thiophene series with alkyllithiums and to give them a theoretical basis. We can nevertheless now assert that the α hydrogen atoms of the thiophene ring have a greater susceptibility to substitution than the β atoms and also than the hydrogen atoms of the side chain in sulfides of structure (I) or (II). It is interesting to note that in sulfide (III) the β-hydrogen atoms can be replaced by metal; in methylphenyl sulfide this property is manifested only by the hydrogen atoms of the methylmercapto group. We hope to reconsider these problems after we have accumulated more experimental data.

EXPERIMENTAL

5-Methylmercapto-2-thiophenecarboxylic acid. 17 ml (0.03 mole) of ethereal solution of n-butyllithium was added to 3.9 g (0.03 mole) of methyl-2-thienyl sulfide in 20 ml ether at 0°. After being stirred for 15 min, the solution was poured into a mixture of dry ice and ether. When the carbon dioxide had evaporated, 20 ml water was added to the mixture with cooling. The aqueous layer was separated and heated for removal of ether. Acidification yielded 4.5 g (86.5%) of acid with m.p. 104°. M.p. 106° after recrystallization from 50% alcohol and heptane.

Found %: C 41.30, 41.50; H 3.51, 3.55; S 36.32, 36.43. $C_6H_6O_2S_2$. Calculated %: C 41.35; H 3.45; S 36.81.

5-Methylmercapto-2-thiophenecarboxylic acid was oxidized with 30% hydrogen peroxide to 5-methylsulfonyl-2-thienylcarboxylic acid, which melted at 198.5—201° after recrystallization from water. *

Found %: C 34.64, 34.49; H 2.95, 2.87; S 31.23, 31.13. $C_6H_6O_4S_2$. Calculated %: C 34.92; H 2.94; S 31.10.

According to the literature [9], 5-methylmercapto-2-thiophenecarboxylic acid has m.p. 106°, and 5-methylsulfonyl-2-thienylcarboxylic acid has m.p. 201—202°.

5-Ethylmercapto-2-thiophenecarboxylic acid. 4 g (0.028 mole) of ethyl-2-thienyl sulfide, reacted as above, gave 4 g (76.6%) of 5-ethylmercapto-2-thiophenecarboxylic acid with m.p. 63°. After recrystallization from 50% alcohol and from heptane the acid melted at 66.5-67°.

Found %: C 44.70, 44.75; H 4.41, 4.37; S 33.76, 33.87. $C_7H_8O_2S_2$. Calculated %: C 44.65; H 4.28; S 34.06.

2,5-Bis(methylmercapto)thiophene. To an ethereal solution of methyl (5-lithium-2-thienyl) sulfide, obtained from 13.0 g (0.1 mole) of methyl-2-thienyl sulfide as described above, was gradually added (with strong cooling) 3.2 g (0.1 mole) of dry, finely pulverized sulfur. The mixture was boiled 45 min; 15.6 g (0.11 mole) of methyl iodide was then added with cooling, and boiling was continued another 6 hr. The mass was then treated (with cooling) with 25% ammonium chloride solution. The ether layer was separated, washed with 0.5 N potassium hydroxide solution and with water and dried with magnesium sulfate. The ether was distilled off and the residue distilled in vacuo to give 10 g (57%) of 2,5-bis(methylmercapto)thiophene with b.p. 123—124° (9 mm), n_D^{20} 1.6365. After redistillation over metallic sodium the product had b.p. 133° (12 mm), n_D^{20} 1.6375.

Metalation of a mixture of thiophene and methyl-2-thienyl sulfide. A mixture of 3.2 g (0.025 mole) of methyl-2-thienyl sulfide and 2.1 g (0.025 mole) of thiophene was metalated at −5° with 0 025 mole n-butyllithium as described above. The aqueous layer was treated with active carbon and acidified with dilute hydrochloric acid. 3.0 g of acid was obtained.

M.p. 82—89°. Neutralization equiv. 170.1; calculated 174.2.

Found %: C 40.70, 40.60; H 3.48, 3.49. $C_6H_6O_2S_2$. Calculated %: C 41.35; H 3.45.

After reprecipitation from active carbon-treated sodium carbonate solution, the acid melted at 104—104.5° (weight 2.7 g). No depression of melting point in admixture with 5-methylmercapto-2-thiophenecarboxylic acid.

Neutralization equiv. 174.5; calc. for $C_6H_6O_2S_2$ 174.2; for $C_5H_4O_2S$ 128.1.

Found %: C 41.60, 41.53; H 3.46; 3.63; S 36.68. $C_6H_6O_2S_2$. Calculated %: C 41.35; H 3.45; S 36.81. $C_5H_4O_2S$. Calculated %: C 46.86; H 3.15; S 25.02.

2-Methylmercapto-5methyl-3-thiophenecarboxylic acid. 3.8 g (0.027 mole) of methyl (5-methyl-2-thienyl-sulfide in 20 ml dry ether and 12 ml (0.027 mole) of ethereal solution of n-butyllithium were stirred at the boil for 30 min. The very darkened solution was poured into a mixture of dry ice and ether; after the usual working-up, a dark oil separated from the aqueous layer; the oil was dissolved in benzene and treated hot with active carbon. From the benzene solution separated 1.35 g (27%) of acid which melted at 193.5° after recrystallization from 50% alcohol and from benzene.

Found %: C 44.44; 44.45; H 4.28, 4.17; S 34.17, 34.51. $C_7H_8O_2S_2$. Calculated %: C 44.65; H 4.28; S 34.06.

From the ethereal solution was separated 1.0 g (26.3%) of the original sulfide. Resinification occurred on boiling; therefore in another experiment the reactants were mixed at 5° and the mixture was stirred 30 min at room temperature; the solution then began to darken; it was poured into a mixture of dry ice and ether. Working up in the usual manner led to separation from the aqueous layer of 0.15 g (2.7%) of 2-methylmercapto-5-methyl-3-thiophenecarboxylic acid with m.p. 193°; the ether layer yielded 85% of the original sulfide. The acid yield was not increased when the reaction was run in tetrahydrofuran.

To 3 g (0.016 mole) of 2-methylmercapto-5-methyl-3-acetothienone and 15 ml of dry pyridine was added 4.1 g (0.016 mole) of iodine; after 45 min heating on a water bath, the solution was stood overnight. The pyridine was taken off in vacuo, and the residue was boiled 1 hr with 3 g sodium hydroxide in 150 ml of 50% alcohol. The

---

*Data supplied by I. F. Shalavina.

cooled solution was diluted with an equal volume of water, extracted with ether and acidified with concentrated hydrochloric acid. The precipitated acid was filtered, washed with water, and dried; yield 1.9 g (62.5 %) with m.p. 188—189° (with decomp.). The acid melted at 193.5—194.5° after recrystallization from ethyl acetate and benzene. No depression of melting point in a mixed test with the acid obtained from methyl (5-methyl-2-thienyl) sulfide by metalation with n-butyllithium followed by carboxylation.

Found %: C 44.59, 44.56; H 4.24, 4.26; S 33.84, 33.66. $C_7H_8O_2S_2$. Calculated %: C 44.66; H 4.28; S 34.06.

5-Methyl-2-thienylmercaptoacetic acid. At 0° n-butyllithium (0.041 mole) in the form of 22 ml of ethereal solution was added to 4 g (0.041 mole) of 2-methylthiophene. The mixture was boiled for 1 hr. Addition was then made (with ice cooling) of 1.3 g (0.04 mole) of dry, finely pulverized sulfur. Boiling was then continued for an hour, and then 6.9 g (0.041 mole) of ethyl bromoacetate was added with cooling (-5 to 0°). The mixture was boiled for another 1.5 hr, stood overnight, and treated (with cooling) with 40 ml of 25% ammonium chloride solution. The ether layer was separated, washed with 0.5 N potassium hydroxide solution and then with water. The ether was driven off and the residue was treated with 2 N alcoholic potassium hydroxide. The precipitated potassium salt was filtered and dried; weight 4.5 g. The aqueous solution of this salt was acidified; an oil separated and was extracted with benzene; the benzene solution was treated with carbon and the benzene was distilled off. The residual oil was dissolved in hot heptane; crystals came down on cooling. The acid melted at 28—29° after recrystallization from heptane.

Found %: C 44.71, 44.80; H 4.22, 4.33; S 34.10, 34.34. $C_7H_8O_2S_2$. Calculated %: C 44.66; H 4.28, S 34.06.

The acid also crystallized after distillation in vacuo and cooling.

2-Ethylmercapto-5-ethyl-3-thiophenecarboxylic acid. 4.6 g (0.027 mole) of ethyl (5-ethyl-2-thienyl) sulfide was metalated with n-butyllithium and carboxylated as described above. 0.42 g (7.3%) of acid was obtained; m.p. 128° after recrystallization from 50% alcohol and from heptane. A mixture with 2-ethylmercapto-5-ethyl-3-thiophenecarboxylic acid prepared by oxidation of 2-ethylmercapto-5-ethyl-3-acetothienone [10] did not exhibit a depression of melting point.

Found %: C 50.18, 50.11; H 5.67, 5.83; S 29.31, 29.26. $C_9H_{12}O_2S_2$. Calculated %: C 49.97; H 5.59; S 29.65.

About 48% of the original sulfide was recovered from the ether layer.

SUMMARY

1. Reaction of alkyl-2-thienyl sulfides with n-butyllithium results in entry of the metal exclusively in the α position of the thiophene ring.

2. 5-Alkyl-2-thienyl sulfide is metalated in low yield in the β position.

3. The alkylmercapto group activates the thiophene nucleus for metalation.

LITERATURE CITED

[1] H. Gilman, D. Shirley, J. Am. Chem. Soc. 71, 1870 (1949); S. Gronowitz, Arkiv Kemi 7, 361 (1954); 8, 441 (1956); Ya. L. Gol'dfarb and M. L. Kirmalova, J. Gen. Chem. 25, 1373 (1955).*

[2] J. D. Roberts and D. Y. Curtin, J. Am. Chem. Soc. 68, 1658 (1946); H. Gilman ed., Organic Syntheses [Russian translation] (For. Lit. Press, 1956), 8, 333. (1956).

[3] S. Gronowitz, Arkiv Kemi 12, 239 (1958).

[4] H. Gilman and F. J. Webb, J. Am. Chem. Soc. 62, 987 (1940).

[5] H. Gilman and F. J. Webb, J. Am. Chem. Soc. 71, 4062 (1949).

[6] D. A. Shirley and E. A. Lehto, J. Org. Ch. 22, 989 (1957).

[7] Ya. L. Gol'dfarb, G. I. Gorushkina and B. P. Fedorov, Bull. Acad. Sci. USSR, Div. Chem. Sci. No. 11 (1959).*

[8] J. Sicé, J. Am. Chem. Soc. 75, 3697 (1953).

[9] J. Cymerman-Craig, J. W. Loder, J. Chem. Soc. 237 (1954).

[10] Ya. L. Gol'dfarb, M. A. Kalik, and M. L. Kirmalova, J. Gen. Chem. 29, 2034 (1959).*

THE SYNTHESIS OF ALIPHATIC AMINO ACIDS FROM THIOPHENE DERIVATIVE

V. γ-AMINO ACIDS FROM 4-NITRO-2-THIOPHENE CARBOXYLIC ACIDS

Ya. L. Gol'dfarb, B. P. Fabrichnyi, and I. F. Shalavina

Institute of Organic Chemistry of the Academy of Sciences USSR

In the first of our investigations [1] on the preparation of aliphatic amino acids by reductive desulfurization (hydrogenolysis) of nitrogen-containing acids of the thiophene series, the behavior of 5-nitro-2-thiophenecarboxylic acid demonstrated the possibility of making use of nitrothiophenecarboxylic acids in this reaction. It must be noted, however, that the yield of the expected δ-aminovaleric acid was extremely small, possibly due in some measure to the complex-forming qualities of nickel *.

In continuation of our investigations, we resolved to study the action of skeletal nickel on a nitro acid containing the nitro group in the β position of the thiophene ring, since the reactivity of thiophene derivatives often changes considerably when the functional group is moved from the α to the β position of the ring. Experiments on the hydrogenolysis of 4-nitro-2-thiophenecarboxylic acids actually revealed that they differ markedly from the above-mentioned 5-nitro-2-thiophenecarboxylic acid in respect to their behavior in presence of skeletal nickel in aqueous medium. 4-Nitro-2-thiophenecarboxylic acids form the corresponding γ-amino acids in satisfactory yield:

$$O_2N \xrightarrow{\text{Ni/H}}[\text{H}_2\text{O}] \quad RCH_2CH(NH_2)CH_2CH_2COOH$$
(I)   (II)
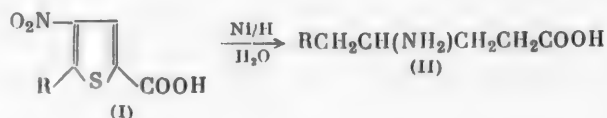
(R = H or normal or branched alkyl). It is known [2] that hydrogenolysis of certain acetylamino acids of the thiophene series leads to products whose yields are higher than in the case of hydrogenolysis of the corresponding amino acids. We therefore decided to conduct the hydrogenolysis of 4-nitro-2-thiophenecarboxylic acids in presence of skeletal nickel in a medium of acetic anhydride in the hope of increasing the yield of aliphatic acetyl-amino acids. Under these conditions the reaction would be expected to take the following course:

$$\xrightarrow{} RCH_2CH(NHCOCH_3)CH_2CH_2COOH$$
(IV)
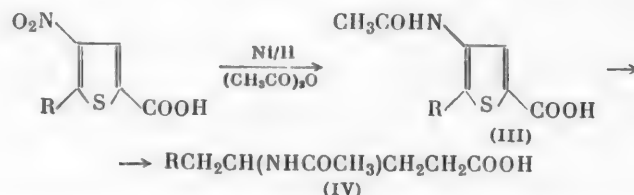
However, only the corresponding acetylamino acids (III)(products of reductive acylation) could be isolated from the mixtures resulting from hydrogenolysis.

Since acetylaminothiophenecarboxylic acids are easily desulfurized in an aqueous medium [2, 3], the limit-ation of the process in acetic anhydride at the stage of formation of (III) may be attributed to the deactivating effect of the anhydride on skeletal nickel as a desulfurization catalyst.

---

*Complex formation is probably responsible for the reaction mass acquiring a crimson color on introduction of skeletal nickel.

In the course of the present work we attempted to reduce 4-nitro-5-methyl-2-thiophenecarboxylic acid (I, R = CH$_3$) with hydrazine hydrate in presence of skeletal nickel under the conditions proposed for reduction of other nitro compounds. This attempt, however, was unsuccessful.

5-Alkyl-2-thiophenecarboxylic acids, required for the synthesis of 4-nitro-5-alkyl-2-thiophenecarboxylic acids, were prepared by oxidation of the corresponding 5-alkyl-2-acetothienones with sodium hypochlorite by the method described for 2-acetothienone [5]. We prepared 5-isobutyl-2-thiophenecarboxylic acid for the first time.

4-Nitro-5-alkyl-2-thiophenecarboxylic acids were prepared by nitration of 5-alkyl-2-thiophenecarboxylic acids with a mixture of nitric and sulfuric acids under the conditions of preparation of 4-nitro-5-methyl-2-thiophene-carboxylic acid [6]. In all of the cases the nitro acid was accompanied by a secondary product in the form of 2,4-dinitro-5-alkylthiophene, which was separated by steam distillation.

4-Nitro-2-thiophenecarboxylic acid (I, R = H) was prepared from 2-thiophenealdoxime via 2-thiophenecarbonitrile. Nitration of the latter gave a mixture of isomeric nitrothiophenecarbonitriles from which 4-nitro-thiophene-carbonitrile was isolated; on hydrolysis it gave the corresponding nitro acid [7].

Hydrogenolysis of the nitro acids was effected with the help of skeletal nickel, which was stored under water; the reaction was carried out in an aqueous mdeium in presence of ammonia solution (to improve the solubility of the nitro acid). In some cases the skeletal nickel could be reused (with a small addition of fresh nickel) without appreciable change in the yield of aliphatic amino acid.

Reductive acetylation of the nitro acids was effected by heating in acetic anhydride with skeletal nickel which had been stored under benzene. The acetylamino acids were purified from resin by dissolution of the residue (remaining after the nickel had been separated and the acetic anhydride had been distilled off) in dilute caustic alkali solution and by acidification of the solution with hydrochloric acid. In the case of reductive acetylation of 4-nitro-2-thiophenecarboxylic acid, the yield of 4-acetamino-2-thiophenecarboxylic acid was extremely minute.

EXPERIMENTAL

2-Isobutyrothienone was prepared in 90% yield by reaction of thiophene with isobutyryl chloride in benzene at 0—5° in presence of tin chloride.

B.p. 108° (15 mm), n_D^{20} 1.5412, d_4^{20} 1.0851. Literature [8]: b.p. 232°.

2-Isobutylthiophene was prepared in 79% yield by reduction of 2-isobutyrothienone with hydrazine hydrate by Kizhner's method as modified by Huang-Minlon [9].

B.p. 173—176°, n_D^{20} 1.4982, d_4^{20} 0.9470. Literature [10]: b.p. 174—176°.

5-Isobutyl-2-acetothienone was obtained in 80% yield by reaction of 2-isobutylthiophene with acetyl chloride in a benzene medium in presence of stannic chloride:

B.p. 146—148° (21 mm), n_D^{20} 1.5349, d_4^{20} 1.0317.

Found %: C 66.01, 65.79; H 7.78, 7.62; S 17.64, 17.63. C$_{10}$H$_{14}$OS. Calculated %: C 65.89; H 7.74; S 17.59.

Semicarbazone: m.p. 204—205° (from alcohol).

Found %: N 17.33, 17.30. C$_{11}$H$_{17}$ON$_3$S. Calculated %: N 17.56.

5-Isobutyl-2-thiophenecarboxylic acid. 86 g chlorine was rapidly passed into a mixture of 660 g ice and a solution of 119 g sodium hydroxide in 170 ml water. The temperature of the solution rose to 75°. At 75—80°, 50 g of 5-isobutyl-2-acetothienone was gradually added with vigorous stirring. After completion of the addition of ketone, stirring was continued until the temperature of the mixture had fallen to 30°. Addition was then made of sodium sulfite until the solution gave a negative reaction to starch—iodide paper. The solution was extracted with ether and filtered; it was then acidified (with cooling) with hydrochloric acid. The precipitate was filtered, washed with water, and dried in a vacuum desiccator over phosphorus pentoxide. The compound was boiled with hexane and the solution was filtered; the filtrate was treated with active carbon and evaporated in vacuo. Yield 42 g (83%) of acid with m.p. 44—45°. 5-Isobutyl-2-thiophenecarboxylic acid melted at 45—46° after recrystallization from water.

Found %: C 58.53, 58.48; H 6.63, 6.57; S 16.74; 16.95. $C_9H_{12}O_2S$. Calculated %: C 58.66; H 6.56; S 17.40.

Oxidation of 5-methyl-2-acetothienone and 5-ethyl-2-acetothienone similarly gave respectively 5-methyl-2-thiophenecarboxylic acid (yield 85% m.p. 136—138° after recrystallization from water; literature [11—15]: m.p. 137°, 138—139°, 137—138°, 138—138.5°, 137—138°) and 5-ethyl-2-thiophenecarboxylic acid (yield 78%, m.p. 66—69°; literature [16—17]: m.p. 71°, 69.5°).

4-Nitro-2-thiophenecarboxylic acid (I, R = H) was prepared [7] by nitration of 2-cyanothiophene, separation of the resulting mixture of nitro compounds, and saponification of 4-nitro-2-thiophenecarbonitrile. Yield of nitro acid 35% reckoned on the mixture of nitrothiophenecarbonitriles, m.p. 150—152° (from water). Literature [7, 12, 18]: m.p. 152°, 154°, 154—155°.

4-Nitro-5-isobutyl-2-thiophenecarboxylic acid (I, R = iso-C_4H_9) was prepared by the method proposed for the synthesis of 4-nitro-5-methyl-2-thiophenecarboxylic acid [6]. To 32 ml of nitric acid (d 1.42) cooled to −7° was added dropwise (with stirring) 18 ml of concentrated sulfuric acid at a temperature not exceeding −5°. To the stirred mixture, at −5°, was added 8.8 g of 5-isobutyl-2-thiophenecarboxylic acid. After the whole of the acid had been added, the mass was stirred for 30 min and then poured into a mixture of crushed ice and water. After the ice had melted, the solution + precipitate was subjected to distillation with steam for separation of 2,4-dinitro-5-isobutylthiophene; the distillate was extracted with ether, and the extract was dried with calcium chloride.

When the aqueous solution was cooled, part of the substance (1.0 g) came down as crystals with m.p. 118—119.5°; the remaining part formed an oil which soon crystallized. Weight 5.5 g, m.p. 109—114°. The two portions of nitro acid were combined and purified by crystallization from water.

The ethereal solutions obtained by extraction of the distillates from three experiments and dried with calcium chloride were combined. After the ether had been driven off, and the residue was distilled in vacuo for separation from resin, 10.0 g of pale-yellow oil was obtained. This was the quantity of 2,4-dinitro-5-isobutylthiophene which had been formed by nitration of 53.4 g of 5-isobutyl-2-thiophenecarboxylic acid. Redistillation gave a fraction (7.6 g) with b.p. 170—175° (9 mm). This fraction gave a deep-blue coloration with alcoholic sodium hydroxide solution; on dilution with water the color changed to violet. This color reaction is characteristic of 2,4-dinitro-thiophenols [19].

Nitration of 5-ethyl-2-thiophenecarboxylic acid similarly gave 4-nitro-5-ethyl-2-thiophenecarboxylic acid (I, R = C_2H_5) together with 2,4-dinitro-5-ethylthiophene. The properties of 4-nitro-5-ethyl-2-thiophenecarboxylic and of 4-nitro-5-isobutyl-2-thiophenecarboxylic acids, as well as of the corresponding 2, 4-dinitro-5-alkylthiophenes, are presented in Table 1.

Nitration of 5-methyl-2-thiophenecarboxylic acid by the method described above gave a 66% yield of 4-nitro-5-methyl-2-thiophenecarboxylic acid (I, R = CH_3), m.p. 179—180° (corr.); literature [6, 12, 20]: m.p. 179—180.5° (corr.), 180—181°, 180—181°; in addition there was obtained (9%) 2,4-dinitro-5-methylthiophene: m.p. 97—98.5°; literature [6,12]: m.p. 98—99° (corr.), 99—100°.

4-Acetylamino-5-isobutyl-2-thiophenecarboxylic acid (III, R = iso-C_4H_9). To a stirred solution of 8.7 g of 4-nitro-5-isobutyl-2-thiophenecarboxylic acid (m.p. 113—116°) in 250 ml of acetic anhydride, heated to 45°, was added 36 g of skeletal nickel which had been stored under benzene. The temperature rose spontaneously to 50°. The mixture was heated to 65° and stirred 20 hr at 70°. The nickel was filtered and washed with hot acetic anhydride and then with acetone. The combined filtrates were evaporated to dryness in vacuo on a water bath. The residue was dissolved in 15% sodium hydroxide solution, filtered from precipitate, and acidified with hdyrochloric acid (congo test). The precipitated acetylamino acid was washed with water and dried in a vacuum desiccator over phosphorus pentoxide. Weight 2.5 g; m.p. 200—202°. A second treatment with caustic alkali of the solid product which had not previously dissolved in alkali and had remained on the filter yielded another 1.1 g of acetylamino acid with m.p. 198—201° (from water).

4-Acetylamino-2-thiophenecarboxylic (III, R = H), 4-acetylamino-5-methyl-2-thiophenecarboxylic (III, R = CH_3) and 4-acetylamino-5-ethyl-2-thiophenecarboxylic (III, R = C_2H_5) acids were similarly prepared.

Methyl ester of 4-acetylamino-2-thiophenecarboxylic acid was prepared by treatment of a suspension of this acylamino acid in ether with an excess of an ethereal solution of diazomethane. It was purified by recrystallization from water.

TABLE 1

Compound	Melting point	Boiling point	Yield %	d_4^{20}	n_D^{20}	Empirical formula	% C		% H		% S	
							found	calc.	found	calc.	found	calc.
4-Nitro-5-ethyl-2-thiophenecarboxylic acid (I, R = C$_2$H$_5$)	156—157°	—	45	—	—	C$_7$H$_7$O$_4$NS	41.35, 41.44	41.78	3.41, 3.47	3.50	15.89, 16.04	15.94
2,4-Dinitro-5-ethylthiophene	—	163—165° (9)	15	1.4284	1.6025	C$_6$H$_6$O$_4$N$_2$S	36.04, 36.22	35.65	3.12, 2.96	2.99	16.05, 15.92	15.86
4-Nitro-5-isobutyl-2-thiophenecarboxylic acid (I, R = iso-C$_4$H$_9$)	119—120	—	60	—	—	C$_9$H$_{11}$O$_4$N S	47.18, 46.90	47.15	5.02, 4.88	4.84	13.88, 14.03	13.99
2,4-Dinitro-5-isobutylthiophene*	—	170—175° (9)	15	—	—	C$_8$H$_{10}$O$_4$N$_2$S	—	—	—	—	—	—

*Found %: N 11.95, 11.82. Calculated %: N 12.17.

The properties of the above acetylamino acids and of the methyl ester of (III, R = H) are given in Table 2.

4-Amino-5-isobutyl-2-thiophenecarboxylic acid hydrochloride. Prepared by boiling 2.6 g of the acetylamino acid with 20 ml dilute (1:1) hydrochloric acid for 2 hr. Crystals came down on cooling and were filtered and dried in vacuo. Weight of unpurified hydrochloride 2.0 g; m.p. 207—210° (decomp.). After recrystallization from a mixture of isopropyl alcohol and ether, 1.6 g of hydrochloride was obtained.

The hydrochlorides of 4-amino-5-methyl-2-thiophene-carboxylic and 4-amino-5-ethyl-2-thiophenecarboxylic acids were similarly prepared. See Table 2 for properties.

4-Amino-5-isobutyl-2-thiophenecarboxylic acid was prepared by the action of the theoretical quantity of sodium carbonate on an aqueous solution of its hydrochloride. It was purified by recrystallization from dilute alcohol. The amino acid is poorly soluble in hot water and much more soluble in hot alcohol. The properties of this amino acid are presented in Table 2.

γ-Amino-ϵ-methylcaprylic aid (II, R = iso-C$_4$H$_9$). To a stirred solution of 8.0 g of 4-nitro-5-isobutyl-2-thiophene-carboxylic acid (I, R = C$_4$H$_9$) (m.p. 113—116°) in 250 ml water and 50 ml concentrated ammonia solution, heated to 45°, was added about 50 g of skeletal nickel. The temperature rose spontaneously to 60°. After it had fallen to 45°, the mixture was heated to 60° and stirred 4 hr at 60—65°. The catalyst was filtered off and washed with hot water. The combined filtrates were evaporated in vacuo; the residue was dried in a vacuum desiccator over phosphorus pentoxide. Weight of unpurified product 5.1 g (yield 84%), m.p. 169—173°; after further recrystallizations from water it had m.p. 173—174°; it crystallizes with one molecule of water.

Hydrogenolysis of the corresponding nitro acids similarly gave γ-aminocaproic (II, R = CH$_3$), γ-aminoenanthic (II, R = C$_2$H$_5$) and γ-aminovaleric (II, R = H) acids.

The hydrochlorides of these amino acids were prepared by dissolution of the acids in hydrochloric acid and evaporation in vacuo; they were purified by recrystallization from a mixture of isopropyl alcohol and acetone.

The benzoyl derivatives were obtained by Schotten—Baumann benzoylation of the amino acids.

Properties of the amino acids and their derivatives are presented in Table 3.

TABLE 2

Compound	Melting point	Yield (%)	Empirical formula	% C found	% C calc.	% H found	% H calc.	% N found	% N calc.	% Cl found	% Cl calc.	% S found	% S calc.
4-Acetylamino-2-thiophene-carboxylic acid (III, R = H)*	273—274° (with decomp)	10	$C_7H_7O_3NS$	45.17, 45.37	45.39	3.74, 3.96	3.81	7.12, 7.25	7.56	—	—	17.00, 17.19	17.31
Methyl ester of 4-acetylamino-2-thiophenecarboxylic acid	135—136	—	$C_8H_9O_3NS$	48.22, 47.98	48.22	4.58, 4.56	4.55	—	—	—	—	15.86, 15.90	16.10
4-Acetylamino-5-methyl-2-thiophenecarboxylic acid (III, R = CH₃)	270—271 (with decomp)	28	$C_9H_9O_3NS$	48.18, 48.24	48.22	4.47, 4.61	4.55	—	—	—	—	15.72, 15.99	16.10
4-Amino-5-methyl-2-thiophene carboxylic acid hydrochloride	252—253 (with decomp)	—	$C_6H_8O_2NClS$	37.69, 37.44	37.21	4.33, 4.14	4.16	7.02, 7.01	7.23	18.21, 18.10	18.31	—	—
4-Acetylamino-5-ethyl-2-thiophenecarboxylic acid (III, R = C₂H₅)	231—232 (with decomp)	13	$C_9H_{11}O_3NS$	50.44, 50.31	50.69	5.23, 4.98	5.20	—	—	—	—	15.17, 15.10	15.04
4-Amino-5-ethyl-2-thiopene-carboxylic acid hydrochloride	257—258 (with decomp)	—	$C_7H_{10}O_2NClS$	40.20, 40.00	40.48	4.65, 4.68	4.85	6.60, 6.81	6.74	—	—	—	—
4-Acetylamino-5-isobutyl-2-thiophenecarboxylic acid (III, R = iso-C4H9)	210—211 (with decomp)	40	$C_{11}H_{15}O_3NS$	54.47, 54.64	54.75	6.15, 6.11	6.27	—	—	—	—	13.13, 13.11	13.29
4-Amino-5-isobutyl-2-thiophene-carboxylic acid hydrochloride	209—210 (with decomp)	—	$C_9H_{14}O_2NClS$	—	—	—	—	5.84, 6.09	5.94	14.79, 15.02	15.04	—	—
4-Amino-5-isobutyl-2-thio-phenecarboxylic acid	170—171 (with decomp)	87	$C_9H_{13}O_2NS$	54.27, 54.10	54.24	6.74, 6.55	6.58	7.14, 7.06	7.03	—	—	16.07, 15.84	16.09

*Literature data [21]; m.p. 272-273°.

TABLE 3

Amino acids and derivatives	Melting point	Yield (%)	Empirical formula	% C		% H		% N	
				found	calculated	found	calculated	found	calculated
γ-Amino-n-valeric acid (II, R = H)*	206—207° (corr.)	72	$C_5H_{11}O_2N$	50.76, 50.95	51.26	9.40, 9.28	9.46	—	—
Benzoyl derivative**	131—133	—	$C_{12}H_{15}O_3N$	—	—	—	—	6.41, 6.37	6.33
γ-Amino-n-caproic acid (II, R = CH₃)***	181—182 (corr.)	76	$C_6H_{13}O_2N$	55.02, 55.11	54.93	10.00, 9.87	9.99	10.54, 10.32	10.68
Benzoyl derivative****	143.5—144.5	—	$C_{13}H_{17}O_3N$	66.16, 66.32	66.36	7.34, 7.20	7.28	5.93, 5.74	5.95
γ-Amino-n-enanthic acid (II, R = C₂H₅)	161—161.5	46	$C_7H_{15}O_2N$	57.66, 57.62	57.90	10.31, 10.31	10.41	9.49, 9.44	9.65
Benzoyl derivative	126—127	—	$C_{14}H_{19}O_3N$	167.42, 67.17	67.45	7.65, 7.69	7.68	5.75, 5.59	5.62
γ-Amino-ε-methylcaprylic acid (II, R = iso-C₄H₉)	173—174 (corr.)	84	$C_9H_{19}O_2N \cdot H_2O$	56.44, 56.43	56.51	10.90, 10.86	11.07	7.29, 7.40	7.32
Benzoyl derivative*****	117—119 (corr.)	—	$C_{16}H_{23}O_3N$	69.16, 60.36	69.29	8.47, 8.38	8.36	5.47, 5.49	5.05
Hydrochloride	155—156	—	$C_9H_{20}O_2NCl$	51.35, 51.50	51.54	9.39, 9.42	9.61	6.61, 6.75	6.68

*Recrystallized from dilute alcohol. Literature [24, 23]: m.p. 132°, 133° (corr.).

**Literature [22, 23]: m.p. 193°-214°.

***Literature [25, 26]: m.p. 180-181°, 187°.

****Literature [25]: m.p. 146.5-147° (corr.).

*****The hydrochloride was recrystallized from a mixture of isopropyl alcohol and acetone. Found %: Cl 16.69, 16.51. Calculated %: Cl 16.91.

SUMMARY

1. A new single-step method of preparation of aliphatic γ-amino acids was developed on the basis of hydrogenolysis of 4-nitro-2-thiophenecarboxylic acids in presence of skeletal nickel. Starting from 4-nitro-2-thiophenecarboxylic, 4-nitro-5-methyl-2-thiophenecarboxylic, 4-nitro-5-ethyl-2-thiophenecarboxylic and 4-nitro-5-isobutyl-2-thiophenecarboxylic acids, the method gave respectively γ-amino-n-valeric, γ-amino-n-caproic, γ-amino-n-enanthic and γ-amino-ε-methylcaprylic acids.

2. Treatment of 4-nitro-2-thiophenecarboxylic, 4-nitro-5-methyl-2-thiophenecarboxylic, 4-nitro-5-ethyl-2-thiophenecarboxylic and 4-nitro-5-isobutyl-2-thiophenecarboxylic acids with excess of skeletal nickel in acetic anhydride did not lead to the expected aliphatic acetylamino acids; the sole identifiable products were products of reductive acylation of nitrothiophenecarboxylic acids, namely 4-acetylamino-2-thiophenecarboxylic, 4-acetylamino-5-methyl-2-thiophenecarboxylic, 4-acetylamino-5-ethyl-2-thiophenecarboxylic and 4-acetylamino-5-isobutyl-2-thiophenecarboxylic acids. Its was consequently established that acetic anhydride deactivates skeletal nickel as a desulfurizing catalyst for 4-nitro-2-thiophenecarboxylic acids.

LITERATURE CITED

[1] Ya. L. Gol'dfarb and B. P. Fabrichnyi, Proc. Acad. Sci. USSR 100, 461 (1955).

[2] Ya. L. Gol'dfarb, B. P. Fabrichnyi and I. F. Shalavina, J. Gen. Chem. 28, 213 (1958).*

[3] N. P. Bun-Hoï and M. Sy, Compt. rend. 242, 2011 (1956).

[4] D. Balcom, A. Furst, J. Am. Chem. Soc. 75, 4334 (1953).

[5] H. D. Hartough. Thiophene and Its Derivatives (Interscience Publishers, Inc. New York, 1952) p. 505.

[6] E. Campaigne, H. Grose, J. Am. Chem Soc. 73, 3812 (1951).

[7] P. Reynaud, K. Delaby, Bull. Soc. Chim. 1955, 1614.

[8] K. Krekeler, Ber. 19, 674 (1886).

[9] Huang-Minlon, J. Am. Chem. Soc. 68, 2487 (1946).

[10] N. P. Buu-Hoï, Ng. Hoan, Ng. D. Xuong, Rec. trav. chim. 71, 285 (1952).

[11] L. E. Levi, Ber. 19, 656 (1886).

[12] I. J. Rinkes, Rec. trav. Chim. 51, 1134 (1932).

[13] H. D. Hartough, L. G. Conley, J. Am. Chem. Soc. 69, 3096 (1947).

[14] J. W. Schick, H. D. Hartough, J. Am. Chem. Soc. 70, 1645 (1948).

[15] M. W. Farrara, R. Levine, J. Am. Chem. Soc. 71, 1496 (1949).

[16] E. Schleicher, Ber. 18, 3015 (1885).

[17] P. Cagniant, D. Cagniant, Bull. Soc. Chim. 1952, 713.

[18] R. Motoyama, S. Nishima, E. Imoto, J. Chem. Soc. Japan, Pure Chem. Soc. 78, 788 (1957); Ref. Zhur. Khim. 1958, 46768.

[19] R. Bonz, Ber. 18, 549 (1885).

[20] H. R. Snyder, L. A. Carpino, J. F. Zack Jr.,J. F. Mills, J. Am. Chem. Soc. 79, 2556 (1957).

[21] W. Steinkopf, P. J. Müller, Lieb. Ann. 448, 210 (1926).

[22] J. Tafel, Ber. 19, 2414 (1886).

[23] E. Fischer, R. Groh, Lieb. Ann. 383, 368 (1911).

[24] L. Senfer, J. Tafel, Ber. 27, 2313 (1894).

[25] A. Müller, E. Feld, Monatsh. 58, 22 (1931).

[26] A. A. Streikheev, S. M. Skuratov, S. M. Shekhter, R. S. Muromova, E. P. Brykina, O. N. Kachinskaya, Proc. Acad. Sci. USSR 102, 543 (1955).

*Original Russian pagination. See C. B. Translation.

THE CHEMISTRY OF SELENEPHONE

XXL. 5-NITRO-2-CYANOSELENOPHENE AND 5-NITRO-2-ACETOSELENOPHENE

Yu. K. Yur'ev and E. L. Zaitseva

Moscow State University

In the preceding papers [1—3] we described the preparation of 5-nitroselenophene-2-aldehyde and a series of its condensation reactions with compounds containing active methylene groups.

In the present work we investigated the possibility of preparation of the simplest ketone of the 2-nitroselenophene series and on the basis of 5-nitroselenophene-2-aldehyde we synthesized 5-nitro-2-acetoselenophene. For this purpose we utilized the procedure described by Walker and Hauser [4] in 1946 for the preparation of p-nitroacetophenone (yield 61%) by reaction of p-nitrobenzoyl chloride with the ethoxymagnesium derivative of malonic ester.

By this method Funahashi and Nishida [5] and Yabuta and Nisida [6] prepared 5-nitro-2-acetylfuran (yield 50%) from 5-nitrofuran-2-carboxylic acid chloride and ethoxymagnesium malonic ester. In the thiophene series the method has been used for the preparation of 3,5-dinitro-2-acetylthiophene (77.6%)[7].

For the preparation of 5-nitro-2-acetoselenophene we converted 5-nitroselenophene-2-carboxylic acid [1] into its acid chloride (by treatment with thionyl chloride), which was reacted with ethoxymagnesium malonic ester to give 5-nitroselenenoyl-2-malonic ester. Hydrolysis of the latter, followed by decarboxylation of the resulting 5-nitroselenenoyl-2-malonic acid, gave 5-nitro-2-acetoselenophene (yield 59% reckoned on the acid and 74.5% reckoned on the acid chloride).

$$O_2N-\underset{Se}{\langle\,\rangle}-COCl \xrightarrow{+C_2H_5OMgCH(COOC_2H_5)_2}$$

$$\rightarrow \left[O_2N-\underset{Se}{\langle\,\rangle}-COC(COOC_2H_5)_2 \right]_2 Mg \xrightarrow[HOH]{H_2SO_4}$$

$$\rightarrow O_2N-\underset{Se}{\langle\,\rangle}-COCH(COOC_2H_5)_2 \xrightarrow[-2CO_2]{hydrolysis} O_2N-\underset{Se}{\langle\,\rangle}-COCH_3$$
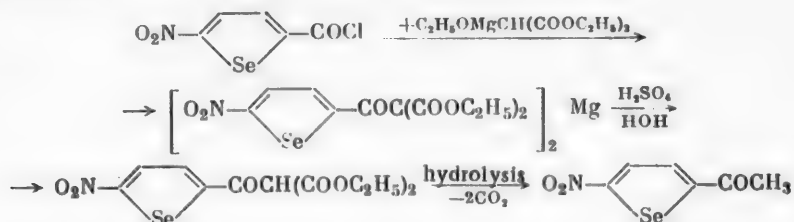
Concerning 5-nitroselenophene-2-carboxylic acid, we prepared it not only by oxidation of 5-nitroselenophene-2-aldehyde, but also by hydrolysis of 5-nitro-2-cyanoselenophene which is formed by dehydration of the oxime of this aldehyde.

EXPERIMENTAL

Oxime of 5-nitroselenophene-2-aldehyde. A mixture of 3.06 g 5-nitroselenophene-2-aldehyde, 1.22 g hydroxylamine hydrochloride, 5.8 g dry pyridine, and 6 ml anhydrous alcohol was heated 2 hr at 110—115°. After the solvents had been taken off in vacuo, the residue was triturated with 12 ml water and the precipitate was separated. Yield 2.26 g (69%) of yellow crystals: m.p. 152—153° (decomp., from methyl alcohol).

Found %: C 27.40, 27.26; H 1.75, 1.89; Se 35.80, 35.73. $C_5H_4O_3N_2Se$. Calculated %: C 27.41; H 1.84; Se 36.04.

5-Nitro-2-cyanoselenophene. A mixture of 1.65 g 5-nitroselenophene-2-aldehyde oxime and 7 g acetic anhydride was refluxed 1 hr in a flask at 165—170° on an oil bath. After cooling, 7 ml water was added and boiling was carried out for 3 min. The mass was neutralized with sodium carbonate and extracted with ether. The ethereal extracts were dried with anhydrous sodium sulfate, the ether was distilled off, and the residue was recrystallized from ligroine. Yield 1.12 g (74%) of yellow crystals with m.p. 90—90.5°.

Found %: C 29.76, 29.58; H 1.19, 1.25; Se 39.01, 39.08. $C_5H_2O_2N_2Se$. Calculated %: C 29.88; H 1.0; Se 39.27.

5-Nitroselenophene-2-carboxylic acid. 0.5 g 5-nitro-2-cyanoselenophene was boiled 3 hr with 4 ml concentrated hydrochloric acid. There was obtained 0.47 g (85.5%), m.p. 188.5—189° (from water); yellow needles. A mixture with authentic 5-nitroselenophene-2-carboxylic acid [1] did not exhibit a depression of melting point.

5-Nitroselenophene-2-carboxylic acid chloride. A mixture of 1.1 g (0.005 mole) 5-nitroselenophene-2-carboxylic acid and 4.1 g (0.034 mole) thionyl chloride in a flask was refluxed for 1.5 hr. After excess of thionyl chloride had been distilled off in vacuo at 50°, there was obtained 0.95 g (80%) of yellow crystals, m.p. 53—53.5° (from chloroform).

Found %: Se 33.27, 33.35. $C_5H_2O_3NClSe$. Calculated %: Se 33.11.

5-Nitroselenophene-2-carboxylic amide. Unpurified 5-nitroselenophene-2-carboxylic acid chloride, obtained as described above, was dissolved in 5 ml dry acetone, and 4 ml of 20% ammonia solution was added dropwise with stirring and cooling. Yield 0.63 g (75%) of yellow needles, m.p. 198.5—199° (from water).

Found %: C 27.15, 27.24; H 2.00, 2.17; Se 35.85, 35.90. $C_5H_4O_3N_2Se$. Calculated %: C 27.42; H 1.84; Se 36.05.

5-Nitro-2-acetoselenophene. 0.32 g (0.013 g-atom) magnesium turnings, 0.6 ml anhydrous alcohol and 0.1 ml dry carbon tetrachloride were placed in a three-necked flask equipped with stirrer, dropping funnel, and calcium chloride tube-topped reflux condenser. Heating of the flask for several minutes at 70—80° led to the start of reaction between magnesium and alcohol. 8 ml of absolute ether was then added in a single portion and (dropwise) a mixture of 2.14 g (0.013 mole) diethyl malonate and 0.6 ml anhydrous ethyl alcohol; stirring was then continued for 3 hr at 40—50° until the whole of the magnesium had dissolved.

At 35° an ethereal solution of impure 5-nitroselenophene-2-carboxylic acid·chloride [obtained from 2.2 g (0.01 mole) acid and 8.2 g thionyl chloride by the above procedure and dissolved in 12 ml absolute ether] was added dropwise to the ethoxymagnesium malonic ester. The mixture was stirred at the same temperature for another hour, cooled, acidified with dilute sulfuric acid (0.8 ml conc. acid in 5.5 ml water), and extracted with ether. The ether was driven off and the residue was heated for 7 hr with a mixture of 3.6 ml glacial acetic acid, 0.45 ml concentrated sulfuric acid and 2.4 ml water; the mass was cooled and poured onto ice and the precipitate was filtered. The latter was treated with a solution of 0.7 g sodium bicarbonate in 14 ml water with heating. After cooling, the product was filtered and washed with glacial acetic acid. Yield 1.29 g (59% reckoned on the 5-nitroselenophene-2-carboxylic acid and 74.5% on the acid chloride) of yellow needles, m.p. 120.5—121° (from ligroine).

Found %: C 33.40, 33.44; H 2.59, 2.49; Se 36.01, 35.97. $C_6H_5O_3NSe$. Calculated %: C 33.06; H 2.31; Se 36.21.

5-Nitro-2-acetoselenophene semicarbazone. 0.55 g of the nitroketone was dissolved by heating in 8 ml alcohol and mixed with a solution of 0.44 g of semicarbazide hydrochloride and 0.55 g sodium acetate in 6 ml water. The mixture was boiled 15 min and cooled. Yield 0.65 g (94.5%) of yellow crystals with m.p. 258—259° (decomp., from alcohol).

Found %: C 30.42, 30.36; H 3.06, 3.03; Se 28.42, 28.48. $C_7H_8O_3N_4Se$. Calculated %: C 30.56; H 2.93; Se 28.69.

SUMMARY

1. Dehydration of 5-nitroselenophene-2-aldehyde oxime leads to 5-nitro-2-cyanoselenophene, hydrolysis of which gives 5-nitroselenophene-2-carboxylic acid. The acid chloride and amide of this acid were also prepared.

2. Reaction of 5-nitroselenophene-2-carboxylic acid chloride with ethoxymagnesium malonic ester gives 5-nitro-2-acetoselenophene.

LITERATURE CITED

[1] Yu. K. Yur'ev and E. L. Zaitseva, J. Gen. Chem. 28, 2164 (1958).[*]

[2] Yu. K. Yur'ev, J. Gen. Chem. 29, 1087 (1959).[*]

[3] Yu. K. Yur'ev and E. L. Zaitseva, J. Gen. Chem. 29, 1965 (1959).[*]

[4] H. Walker and C. Hauser, J. Am. Chem. Soc. 68, 1387 (1946).

[5] S. Funahashi and S. Nishida, J. Sci. Reserach. Inst. (Tokyo) 45, 108, (1951); C. A. 46, 4524 (1952).

[6] Jap Patent 4534 (1955); Ref. Zhur. Khim. 1958, 347.

[7] M. Bellenghi, G. Carrara, F. Fava, E. Ginoulhiac, C. Martinuzzi, A. Vecchi, and E. Weitnauer, Gazz. 82, 773 (1952).

---

[*]Original Russian pagination. See C. B. Translation.

THE CHEMISTRY OF SELENOPHENE

XXII. AMINOMETHYLATION AND ACYLAMINOMETHYLATION OF SELENOPHENE AND ITS HOMOLOGS

Yu. K. Yur'ev, N. K. Sadovaya, and A. B. Ibragimova
Moscow State University

In one of the preceding papers [1] we reported the aminomethylation of ketones of the selenophene series and the preparation by this route of hydrochlorides of β-dimethylaminoalkyl-(alkylselenenyl-2)-ketones. In the present work we applied the aminomethylation reaction to selenophene itself and its homologs.

In the thiophene series this reaction, which makes use of the mobility of the hydrogen atoms at the α carbon atoms of the ring, takes place on treatment with ammonium chloride and 30% formalin [2, 3]; formalin can be replaced by hexamethylenetetramine or paraformaldehyde [3, 4]. The reaction with thiophene proceeds with intermediate formation of N-(2-thenyl)-formaldimine and leads to 2-thenylamine, di(2-thenylamine) and a large quantity of resinous substances which are probably polymers [5]. Hydrochlorides of alkylamines (methylamine and dimethylamine) could not be reacted: aminomethylation did not take place with them [6] and thienylmethanes were formed instead of thenylamines. For example, 2-methylthiophene, formaldehyde, and dimethylamine hydrochloride gave di-(5-methyl-2-thienyl)-methane (45%) [4]. Regarding acylaminomethylation reactions, shortly after the preparation by Sachs [7] of the first of the methylolacylamides (methylolphthalimide) Einhorn [8] effected their condensation with some aromatic compounds in presence of sulfuric acid; the condensing agent used by Nenitescu and Dinulescu [9] in this reaction was a mixture of concentrated sulfuric acid and glacial acetic acid. Acylaminomethylation of thiophene was performed by Hartough [10] in presence of 85% phosphoric acid.

In the present work we studied the dialkylaminomethylation of selenophene by the action of dimethylamine hydrochloride and paraformaldehyde in a medium of anhydrous alcohol, i.e. under the conditions employed for the aminomethylation of ketones of the selenophene series [1]. We were able to show that in this method of aminomethylation of selenophene and its homologs the reaction does not go in the direction of formation of selenenylmethanes (as was to be feared by analogy with the behavior of thiophene) but in the direction of formation of the corresponding hydrochlorides of β-dimethylaminomethylalkylselenophenes in yields of up to 60% (in the case of selenophene itself the yield was only 30%.

$$\text{(selenophene)} + (CH_2O)_n + (CH_3)_2NH \cdot HCl \longrightarrow \text{(selenophene)}-CH_2N(CH_3)_2 \cdot HCl.$$
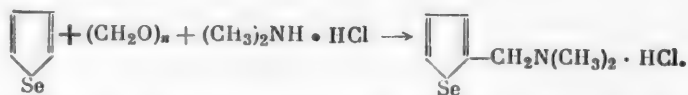
In this manner we prepared the hydrochlorides of 2-(dimethylaminomethyl) selenophene, 3-methyl-2-(dimethylaminomethyl) selenophene, 2,4-dimethyl-5-(dimethylaminomethyl) selenophene, and 3,4-dimethyl-2-(dimethylaminomethyl) selenophene. The free bases— 2-(dimethylaminomethyl) selenophene and 3-methyl-2-(dimethylaminomethyl) selenophene—were prepared by passing dry ammonia into a suspension of the hydrochlorides in absolute ether. An unsuccessful attempt was made to carry out aminomethylation with ammonium chloride (in place of dimethylamine hydrochloride) and paraformaldehyde under the same conditions (i.e. in a medium of anhydrous alcohol). The selenophene did not enter into reaction. We synthesized aminomethylselenophenes by the procedure developed for thiophene [3, 4], i.e. we subjected selenophene and 2-methylselenophene to the action of ammonium chloride and 36% formalin or paraformaldehyde. In both cases aminomethylation of selenophene went with formation of resinous polymers. We obtained the best results when using 36% formalin; 2-selenenylamine

(2-aminomethylselenophene) and 2-methyl-5-selenenylamine (2-methyl-5-aminomethylselenophene) were obtained in 20.5% yields.

$$R-\underset{Se}{\boxed{}} + CH_2O + NH_4Cl \rightarrow R-\underset{Se}{\boxed{}}-CH_2NH_2.$$
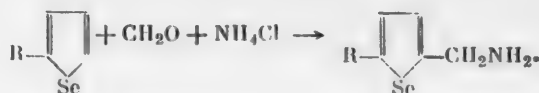
Oxidation of their alkaline solution with potassium permanganate gave the corresponding selenophene carboxylic acids.

We studied the acylaminomethylation reaction in the selenophene series with reference to the condensation of selenophene with methylolbenzamide, methylolacetamide, and methylolphthalimide, but only in the first case did we obtain definite results. Catalysts tested were sulfuric acid, a mixture of sulfuric and glacial acetic acids, and 85% phosphoric acid. Acylaminomethylation does not take place in presence of sulfuric acid; an amorphous substance was obtained; this was apparently a polymeric sulfur compound of selenophene. In presence of phosphoric acid we found conditions in which selenophene condenses with methylolbenzamide in 50—60% yield; the reaction readily goes as far as formation of di(N-benzoylaminomethyl) selenophene even with a deficiency of methylolbenzamide. Formation of di-derivatives of selenophene is apparently due to the selenophene nucleus being very strongly activated by the first N-benzoylaminomethyl group. In this manner we obtained 2,5-di-(N-benzoylaminomethyl)-selenophene, 3-methyl-2,5-di(N-benzoylaminomethyl)selenophene, 2,5-dimethyl-3,4-di(N-benzoylaminomethyl)selenophene, and 3,4-dimethyl-2,5-di-(N-benzoylaminomethyl)selenophene.

$$\underset{Se}{\boxed{}} + 2C_6H_5CONHCH_2OH \rightarrow C_6H_5CONHCH_2-\underset{Se}{\boxed{}}-CH_2NHCOC_6H_5.$$
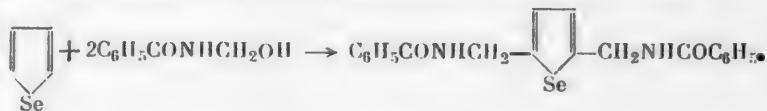
2-Methylselenophene gave both a mono- and a di(N-benzoylaminomethyl derivative— 2-methyl-5-(N-benzoylaminomethyl)selenophene and 2-methyl-4,5-di(N-benzoyl aminomethyl)selenophene.

$$CH_3-\underset{Se}{\boxed{}} + 3C_6H_5CONHCH_2OH \rightarrow CH_3-\underset{Se}{\boxed{}}-CH_2NHCOC_6H_5 +$$

$$+ CH_3-\underset{Se}{\boxed{}}\genfrac{}{}{0pt}{}{-CH_2NHCOC_6H_5}{-CH_2NHCOC_6H_5}$$
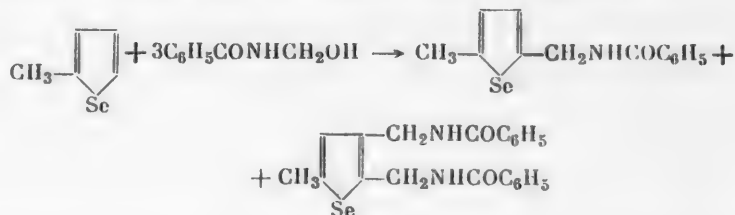
2-Methyl-5-(N-benzoylaminomethyl)selenophene was found to be identical with the benzoyl derivative of 2-methyl-5-selenenylamine obtained by aminomethylation of 2-methylselenophene with formalin and ammonium chloride (m.p. 121—122°); it was markedly different from the benzoyl derivative of 2-(β -aminoethyl)selenophene (m.p. 70—71°) [11]; a melting point depression was observed in admixture with the latter (m.p. 105—106°).

Attempts to remove the benzoyl groups and to prepare the free bases from the N-benzoylaminomethylselenophenes were unsuccessful both on acidic and on alkaline hydrolysis; in both of the cases the only reaction was resinification of the selenophene ring with liberation of selenium.

EXPERIMENTAL

Hydrochlorides of dimethylaminomethylalkylselenophenes were prepared by our procedure for the synthesis of β -dimethylaminoalkyl-(selenenyl-2)ketones [1]; they were purified by reprecipitation from alcohol by ether.

2-(Dimethylaminomethyl)selenophene hydrochloride. 1.5 g (0.011 mole) of selenophene, 1.5 g (0.018 mole) dimethylamine hydrochloride, 0.75 g (0.025 mole) paraformaldehyde and 3 ml anhydrous alcohol gave 0.8 g (30%); m.p. 178—179'.

Found %: C 37.30, 37.23; H 5.34, 5.17; N 5.79, 5.84. $C_7H_{12}NClSe$. Calculated %: C 37.44; H 5.39; N 6.24.

<u>3-Methyl-2-(dimethylaminomethyl)selenophene hydrochloride</u>. 1 g (0.007 mole) 3-methylselenophene, 1.21 g (0.015 mole) dimethylamine hydrochloride, 0.6 g (0.02 mole) paraformaldehyde and 3 ml anhydrous alcohol gave 1 g (60%); m.p. 209—210°.

Found %: C 40.11, 40.07; H 6.09, 5.97; N 5.45, 5.49. $C_8H_{14}NClSe$. Calculated %: C 40.44; H 5.89; N 5.85.

<u>2,4-Dimethyl-5-(dimethylaminomethyl)selenophene</u>. 3.2 g (0.02 mole) 2,4-dimethylselenophene, 2.4 g (0.03 mole) dimethylamine hydrochloride, 1.35 g (0.045 mole) paraformaldehyde and 5 ml anhydrous alcohol gave 3.1 g (61%); m.p. 184—185°.

Found %: C 42.93, 42.90; H 6.67, 6.72; N 5.34, 5.34. $C_9H_{16}NClSe$. Calculated %: C 42.80; H 6.39; N 5.55.

<u>3-4-Dimethyl-2-(dimethylaminomethyl)selenophene</u>. 1.6 g (0.01 mole) 3,4-dimethylselenophene, 1.2 g (0.015 mole) dimethylamine hdyrochloride, 0.7 g (0.02 mole) paraformaldehyde and 3 ml anhydrous alcohol gave 1.6 g (61%); m.p. 199—200°.

Found %: C 42.64, 42.49; H 6.35, 6.32; N 5.54, 5.62. $C_9H_{16}NClSe$. Calculated %: C 42.80; H 6.39; N 5.55.

<u>2-(Dimethylaminomethyl)selenophene</u>. Passage of dry ammonia into a suspension of 1.8 g of 2-(dimethylamino-methyl)selenophene hydrochloride in absolute alcohol gave 0.75 g (50%) of the base.

B.p. 82—82.5° (14 mm), n_D^{20} 1.5460, d_4^{20} 1.3119, MR_D 45.43. $C_7H_{11}NSeF_2$. Calculated %: 45.94.
Found %: C 44.43, 44.21; H 6.10, 5.96. $C_7H_{11}NSe$. Calculated %: C 44.70; H 5.89.

<u>2-(Dimethylaminomethyl)-3-methylselenophene</u>. 1.9 g of 3-methyl-2-(dimethylaminomethyl)selenophene hydrochloride, treated as above, gave 0.7 g (44%).

B.p. 97.5—98° (16 mm), n_D^{20} 1.5422, d_4^{20} 1.2591, MR_D 50.53. $C_8H_{13}NSeF_4$. Calculated %: 50.55.
Found %: C 47.53, 47.51; H 6.76, 6.84. $C_8H_{13}NSe$. Calculated %: C 47.73; H 6.48.

<u>2-Selenenylamine</u>. 40 g (0.48 mole) of 36% formalin and 12.8 g (0.24 mole) of ammonium chloride were added to 15 g (0.12 mole) of selenophene in a three-necked flask fitted with a powerful stirrer, a reflux condenser, and a thermometer. The mixture was heated to 60° — the temperature of commencement of the reaction— and it was held at 64—65° for half an hour. It was then cooled to 18—20°; 35 ml methyl alcohol was added and stirring was continued for another 2 hr. The mass was then stood overnight. The solvent and unchanged selenophene (2 g) were distilled off with steam and the residue in the flask was neutralized with 24 ml (0.24 mole) of 40% sodium hydroxide solution. The precipitate of 15 g (79%), containing selenium and isoluble in organic solvents, was filtered and washed with ether. It changed into a resinous mass after being twice dissolved in 2 N hydrochloric acid and reprecipitated with 25% ammonia.

The filtrate was saturated with common salt and repeatedly extracted with ether. The ether extracts were dried with potassium carbonate. After removal of the ether, the substance was distilled in vacuo to give 3.3 g (20.5%) of 2-selenenylamine.

B.p. 89.5—90° (10 mm), n_D^{20} 1.6021, d_4^{20} 1.5512, MR_D 35.37. $C_5H_7NSeF_2$. Calculated %: 36.15.
Literature [12]: b.p. 103—103.5° (15 mm), n_D^{20} 1.6044, d_4^{20} 1.5530.
Found %: C 37.73, 37.54; H 4.54, 4.42. C_5H_7NSe. Calculated %: C 37.52; H 4.41.

2-Selenenylamine carbonate (easily formed in the air): m.p. 88—89°.

Found %: Se 41.61, 41.57. $C_{11}H_{16}O_3N_2Se$. Calculated %: Se 41.76.

<u>2-(N-Benzoylaminomethyl)selenophene</u>. 0.47 g (0.003 mole) 2-selenenylamine, 0.32 g (0.008 mole) sodium hydroxide and 0.5 g (0.003 mole) benzoyl chloride gave 0.62 g (80%): m.p. 121—122° (from toluene).

Found %: Se 29.87, 29.53. $C_{12}H_{11}ONSe$. Calculated %: Se 29.85.

<u>Selenophene-2-carboxylic acid</u>. Following the procedure of Rinkes [13, 14], 1.94 g (0.012 mole) $KMnO_4$ in 40 ml water was stirred slowly at 40° into 0.97 g (0.006 mole) 2-selenenylamine and 1.94 g (0.048 mole) sodium hydroxide in 25 ml water. After standing for 24 hr, the manganese dioxide was filtered off and washed with

hot water. The filtrates were evaporated and acidified with 20% hydrochloric acid to give a total of 0.65 g (61%), m.p. 119−120° (from water); no depression in a mixed melting point test with authentic selenophene-2-carboxylic acid [15].

2-Methyl-5-selenenylamine. A mixture of 7.5 g (0.052 mole) of 2-methylselenophene, 4.2 g (0.078 mole) of ammonium chloride and 4.3 g (0.052 mole) of 36% formalin was stirred at 40°; the temperature rose spontaneously to 51°, and stirring was continued for 50 min at this temperature. After cooling to 18−20°, 6 ml of benzene was added and the mass was neutralized with 8 ml of 40% sodium hydroxide solution; an oil was formed which changed into a resin (0.31 g); this contained selenium and was insoluble in organic solvents. The filtrate was saturated with common salt and repeatedly extracted with benzene. The benzene was driven off and the residue distilled in vacuo to give: a) 0.65 g of unchanged 2-methylselenophene and b) 1.7 g (20.5%) of amine.

B.p. 93−93.5° (7 mm) n_D^{20} 1.5742, d_4^{20} 1.4172, MR_D 40.53. $C_6H_9NSeF_2$. Calculated %: 40.77.
Found %: C 41.33, 41.15; H 5.40, 5.33. C_6H_9NSe. Calculated %: C 41.37; H 5.21.

2-Methyl-5-selenenylamine carbonate (easily formed in the air): m.p. 83−84° (decomp.).

Found %: Se 38.81, 38.68. $C_{13}H_{20}O_3N_2Se_2$. Calculated %: Se 38.91.

2-Methyl-5-(N-benzoylaminomethyl)selenophene. 0.36 g (0.002 mole) of 2-methyl-5-selenenylamine, 0.2 g (0.005 mole) of sodium hydroxide and 0.3 g (0.002 mole) of benzoyl chloride gave 0.37 g (65%): m.p. 132−133° (from toluene). No depression in a mixed melting point test with a preparation obtained by benzoyl-aminomethylation of 2-methylselenophene.

2-Methylselenophene-5-carboxylic acid. Starting from 1 g (0.004 mole) of 2-methyl-5-selenenylamine, 2 g (0.048 mole) of potassium permanganate and 2 g (0.012 mole) of sodium hydroxide in 100 ml water, reaction by the above procedure gave 0.9 g (84%) of product with m.p. 134−134.5° (from water).

Literature [16]: m.p. 134−136°.
Found %: C 37.89, 37.71; H 3.15, 3.25. $C_6H_6O_2Se$. Calculated %: C 38.11; H 3.20.

Procedure for N-benzoylaminomethylation of selenophene and its homologs. 0.03 mole of selenophene, 0.06 mole of methylolbenzamide and 15 ml of glacial acetic acid were put into a three-necked flask (fitted with stirrer, reflux condenser, and thermometer) and the mixture was heated to 70° on a water bath. 0.003 mole of 85% phosphoric acid in 10 ml of glacial acetic acid was added dropwise at 70−80°, and heating was continued for 12−15 hr at this temperature. The mass was then cooled and poured onto ice. An oil separated and gradually solidified. It was collected and recrystallized. The filtrate was extracted with ether to remove unchanged selenophene. Part of the selenophene resinified and methylenedibenzamide was formed in the course of the work.

2,5-Di(N-benzoylaminomethyl)selenophene. 10 g selenophene and 22.6 g methylolbenzamide were treated with 0.8 g 85% phosphoric acid and 30 ml glacial acetic acid to give 14 g (60.5%) of product with m.p. 165−166° (from benzene).

Found %: C 60.89, 60.95; H 4.77, 4.75; Se 19.47, 19.48. $C_{20}H_{18}O_2N_2Se$. Calculated %: C 60.46; H 4.57; Se 19.87.

3-Methyl-2,5-di(N-benzoylaminomethyl)selenophene. 3 g 3-methylselenophene and 6.2 g methylolbenzamide in presence of 0.2 g (85%) phosphoric acid and 15 ml glacial acetic acid gave 3.5 g (52%) of product with m.p. 198−199° (from benzene).

Found %: C 61.56, 61.66; H 4.89, 5.02; Se 19.15, 19.23. $C_{21}H_{20}O_2N_2Se$. Calculated %: C 61.32; H 4.90; Se 19.24.

2,5-Dimethyl-3,4-di(N-benzoylaminomethyl) selenophene. 5.4 g 2,5-dimethylselenophene and 10 g methylol-benzamide in presence of 0.3 g (85%) phosphoric acid and 25 ml glacial acetic acid gave 7.5 g (48%) of product with m.p. 201−202° (from benzene).

Found %: 62.20, 62.16; H 5.29, 5.43. $C_{22}H_{22}O_2N_2Se$. Calculated %: C 62.10; H 5.21.

3,4-Dimethyl-2,5-di(N-benzoylaminomethyl)selenophene. 6.75 g 3,4-dimethylselenophene and 12.8 g methylol-benzamide in presence of 0.4 g (85%) phosphoric acid and 25 ml glacial acetic acid gave 9 g (50%) of product with m.p. 224−225° (from benzene).

Found %: C 61.83, 62.03; H 4.94, 5.14; Se 18.58, 18.49. $C_{22}H_{22}O_2N_2Se$. Calculated %: C 62.10; H 5.21; Se 18.74.

Benzoylaminomethylation of 2-methylselenophene. 5 g of 2-methylselenophene and 15.3 g of methylol-benzamide in presence of 0.33 g of 85% phosphoric acid and 25 ml of glacial acetic acid gave 6.7 g (48%) of 2-methyl-4,5-di(N-benzoylaminomethyl)selenophene with m.p. 181-181.5° (from benzene).

Found %: C 61.27, 61.39; H 5.05, 5.11; Se 19.14, 19.46. $C_{21}H_{20}O_2N_2Se$. Calculated %: C 61.32; H 4.90; Se 19.21.

From the reaction product was also isolated 1.5 g (16%) of 2-methyl-5(N-benzoylaminomethyl)selenophene with m.p. 132—133° (from toluene).

Found %: C 55.98, 56.13; H 4.92, 5.02. $C_{13}H_{13}ONSe$. Calculated %: C 56.13; H 4.71.

There was no depression of melting point in a mixed test with the product of benzoylation of 2-methyl-5-selenenylamine.

SUMMARY

1. Dialkylaminomethylation of selenophene and its homologs by the action of dimethylamine hydrochloride and paraformaldehyde in a medium of ethanol leads to hydrochlorides of dimethylaminomehtylselenophenes in yields of 30—60%. The dimethylaminomethyl group enters in the α position of the selenophene ring.

2. Aminomethylation of selenophene and of 2-methylselenophene by the action of 36% formalin and ammonium chloride leads to 2-selenenylamine and 2-methyl-5-selenenylamine respectively.

3. Benzoylaminomethylation of selenophene and its homologs in presence of 85% phosphoric acid leads predominantly to di-N-benzoylaminomethyl derivatives of selenophene (50—60%); the N-benzoylaminomethyl groups enter at the β position of the selenophene ring if the α position is occupied.

LITERATURE CITED

[1] Yu. K. Yur'ev and N. K. Sadovaya, J. Gen. Chem. 27, 1587 (1957).*

[2] H. Hartough, S. Lukasiewiez, and E. Murray, J. Am. Chem. Soc. 68, 1389 (1946).

[3] H. Hartough and S. Meisel, J. Am. Chem. Soc. 70, 4018 (1948).

[4] H. Hartough, S. Lukasiewiez, and E. Murray, J. Am. Chem. Soc. 70, 1146 (1948).

[5] H. Hartouch, S. Meisel, E. Koft, and J. Schick, J. Am. Chem. Soc. 70, 4013 (1948).

[6] H. Hartough, J. Schick, and J. Dickert, J. Am. Chem. Soc. 72, 1572 (1950).

[7] F. Sachs, Ber. 31, 3230 (1898).

[8] A. Einhorn, Lieb. Ann. 343, 207 (1905); 361, 113 (1908).

[9] C. Nenitescu, J. Dinulescu, Comun. Acad. R. P. Romane 4, No. 1—2, 45 (1954).

[10] H. Hartough, Thiophene and its Derivatives. (New York, 1952) p. 253.

[11] Yu. K. Yur'ev, N. N. Mezentsova, and V. E. Vas'kovskii, J. Gen. Chem. 29, 3239 (1959).*

[12] Yu. K. Yur'ev and N. N. Mezentsova, J. Gen. Chem. 28, 3041 (1958).*

[13] J. Rinkes, Rec. trav. chim. 63, 543 (1944).

[14] H. Hartough and J. Dickert, J. Am. Chem. Soc. 71, 3922 (1949).

[15] Yu. K. Yur'eva and N. K. Sadovaya, J. Gen. Chem. 26, 3154 (1956);* 28, 2162 (1958).*

[16] E. G. Kataev and M. V. Palkina, Sci. Memoirs Kazan Univ. 113, 8, 115 (1953).**

Received November 4, 1958

* Original Russian pagination. See C. B. Translation.
** In Russian.

TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

XXV. ACYLOXYTRICHLOROSILANES FROM ORGANIC ALIPHATIC ACIDS

Yu. K. Yur'ev, Z. V. Belyakova, and V. P. Volkov

In our preceding communications [1, 2] we showed that heating of acids of the aromatic and heterocyclic series with excess of silicon tetrachloride leads to quantitative formation of acyloxytrichlorosilanes. These compounds disproportionate (symmetrize)— some after standing for fairly lengthy periods, others after a few hours, but all without exception rapidly when heated — to form tetraacyloxysilanes and silicon tetrachloride.

The failure of Goubeau and Mundiel [3] to obtain acetoxytrichlorosilane by the action of excess of silicon tetrachloride on acetic acid (only tetraacetoxysilane was obtained) was due, as we established, to the facility with which acetoxytrichlorosilane disproportionates to tetraacetoxysilane and silicon tetrachloride. This was the only reason why the cited authors could not even detect the formation of acetoxytrichlorosilane.

In the present work we established that heating of fatty acids – including acetic acid— with excess of silicon tetrachloride leads to the corresponding acyloxytrichlorosilanes (I) in quantitative yields. They are colorless liquids which fume in the air and readily disproportionate on distillation (II).

$$\text{RCOOH} + \text{SiCl}_4 \longrightarrow \text{RCOOSiCl}_3 + \text{HCl} \qquad \text{(I)}$$

$$4\text{RCOOSiCl}_3 \longrightarrow \text{Si(OCOR)}_4 + 3\text{SiCl}_4 \qquad \text{(II)}$$

Acetoxytrichlorosilane disproportionates the most easily. The tendency of acyloxytrichlorosilanes formed by fatty acids to disproportionate decreases with increasing length of the carbon chain and and also with increasing degree of branching of the chain. This regularity is illustrated by the table, which gives the yields of acyloxytrichlorosilanes obtained on their distillation. Acyloxytrichlorosilanes break down on distillation at atmospheric pressure to form acid chlorides (17—42%), whereas the product of breakdown when the distillation is performed in vacuo is the acid anhydride (21—38%). These facts support our earlier theory of the thermal breakdown of acyloxytrichlorosilanes [2], according to which heating is accompanied by disproportionation to silicon tetrachloride and tetraacyloxysilane (II) with subsequent breakdown of the tetraacyloxysilane to silica and acid anhydride (III); the latter reacts with silicon tetrachloride to form the acid chloride and silica (IV).

$$\text{Si(OCOR)}_4 \longrightarrow 2(\text{RCO})_2\text{O} + \text{SiO}_2 \qquad \text{(III)}$$

$$2(\text{RCO})_2\text{O} + \text{SiCl}_4 \longrightarrow 4\text{RCOCl} + \text{SiO}_2 \qquad \text{(IV)}$$

Vacuum distillation of the acyloxytrichlorosilane naturally results in the last step— formation of acyl chloride by reaction between acid anhydride and silicon tetrachloride— not taking place, due to volatilization of the silicon tetrachloride, so that the reaction terminates with formation of anhydride.

In the preceding paper [1] we showed, with reference to the reaction of benzoyloxytrichlorosilane with an equimolar quantity of anhydrous ethanol at -30°, that the benzoyloxy group is more easily replaced than chlorine atoms by the ethoxy group. This was confirmed in the present work in the reaction of molar quantities of 2-furoyloxy- and 2-thenoyloxytrichlorosilane with anhydrous ethanol under the same conditions: yields of 2-furoic acid and thiophene-2-carboxylic acid were 72 and 66% respectively.

$$\text{RCOOSiCl}_3 + \text{C}_2\text{H}_5\text{OH} \longrightarrow \text{RCOOH} + \text{C}_2\text{H}_5\text{OSiCl}_3,$$
$$\text{R} = \alpha\text{-C}_4\text{H}_3\text{O}, \quad \alpha\text{-C}_4\text{H}_3\text{S}.$$
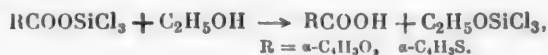
If the reactivities of the groups in question had been identical, the yield of each acid should have been only 25%. This unusual behavior of the acyloxy group is evidently due to the catalytic influence of hydrogen chloride, which is released in the secondary reaction of replacement of halogen by alkoxyl.

$$RCOOSiCl_3 + C_2H_5OH \longrightarrow RCOOSiCl_2(OC_2H_5) + HCl$$

We also established that the action of acetic acid on 2-furoyloxy- and on 2-thenoyloxytrichlorosilane is accompanied by replacement of halogen atoms by acetoxy groups with formation of 2-furoyloxytriacetoxysilane (96%) respectively. Consequently, the action of organic acids on acyloxytrichlorosilanes is a means of preparation of previously undescribed mixed anhydrides formed by silicic acid and two organic acids.

$$RCOOSiCl_3 + 3CH_3COOH \longrightarrow RCOOSi(OCOCH_3)_3 + 3HCl$$
$$R = \alpha\text{-}C_4H_3O, \ \alpha\text{-}C_4H_3S.$$
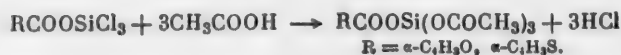
Acyloxytrichlorosilanes, like tetraacyloxysilanes [4], react with organomagnesium compounds to give tetra-alkylsilanes (53—79%) and tertiary alcohols (74—89%).

$$RCOOSiCl_3 + 6R'MgX \longrightarrow \begin{matrix} R' \\ | \\ R-C-OH \\ | \\ R' \end{matrix} + SiR_4,$$

1) $R = CH_3$, $R' = C_2H_5$, C_3H_7, C_4H_9;
2) $R = C_4H_3O$, $R' = C_2H_5$;
3) $R = C_7H_{15}$, $R' = C_4H_9$.

EXPERIMENTAL

Acyloxytrichlorosilanes were prepared, as described previously [1, 2], by the action of excess of silicon tetrachloride on fatty acids. The yields of acyloxytrichlorosilanes are quantitative, as indicated by the date for analysis of the undistilled acetoxytrichlorosilane (only after vacuum distillation of excess silicon tetrachloride). The table lists the acyloxytrichlorosilanes that we prepared and the products of their breakdown during normal distillation and distillation in vacuo.

Reaction with ethyl alcohol. 1. Using the earlier procedure [1], 2.3 g (0.05 mole) of anhydrous ethanol was reacted at -30° with 12.3 g (0.05 mole) of 2-furoyloxytrichlorosilane to give 4.0 g (72%) of 2-furoic acid with m.p. 130—131°; no depression of melting point in a mixed test with authentic 2-furoic acid. Distillation of the filtrate yielded 4.6 g of a fraction with b.p. 100—140° (752 mm); this boiling range corresponded to a mixture of ethoxytrichlorosilane and diethoxydichlorosilane.

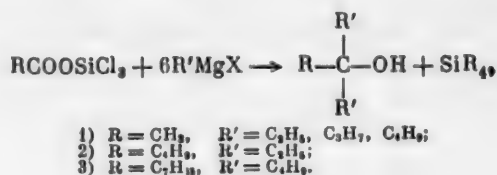2. Reaction at -30° of 2.3 g (0.05 mole) anhydrous ethanol with 13.2 g (0.05 mole) 2-thenoyloxytrichlorosilane led to separation of 4.2 g (66%) of thiophene-2-carboxylic acid with m.p. 124—125°; no depression in admixture with authentic thiophene-2-carboxylic acid. Distillation of the filtrate gave 4.1 g of a fraction with b.p. 100—140° (749 mm).

Reaction with organic acids. A mixture of 0.05 mole acyloxytrichlorosilane and 0.15 mole glacial acetic acid was heated in a 50 ml flask fitted with a reflux condenser for 4—5 hr at 40—60° and 5—10 min on a boiling water bath until hydrogen chloride ceased to come off. The mass crystallized on cooling. The crystals were washed with ligroine and analyzed.

1. From 12.3 g of 2-furoyloxytrichlorosilane and 9.0 g of acetic acid was obtained 15.2 g (96%) of 2-furoyloxytriacetoxysilane with m.p. 80—81.5°.

Found %: Si 8.76, 8.83. $C_{11}H_{12}O_9Si$. Calculated %: Si 8.88.

2. From 13.2 g of 2-thenoyloxytrichlorosilane and 9.0 g of acetic acid was obtained 15.9 g (95%) of 3-thenoyloxytriacetoxysilane with m.p. 65—67°.

Found %: Si 8.32, 8.38. $C_{11}H_{12}O_8SSi$. Calculated %: Si 8.45.

Reaction with organomagnesium compounds. 0.05 mole of acyloxytrichlorosilane in 25 ml of absolute ether was added to the Grignard reagent from 12.2 g (0.5 g-atom) of magnesium and 0.5 mole of alkyl halide in 175 ml

Acyl group	Acyloxytrichlorosilanes						Products of breakdown during distillation			
	boiling point (pressure in mm)	yield after distillation (in %)	% Si		% Cl		name	yield (%)	boiling point (pressure in mm)	n_D^{20}
			found	calculated	found	calculated				
Acetyl	129—130° (752) *	36	14.18, ** 14.23 ** 14.33, 14.39	14.51	54.71, ** 54.78 ** 55.18, 55.22	55.00	—	—	—	—
Propionyl	149—150 (749)	41	13.42, 13.46	13.53	51.18, 51.33	51.24	Propionyl chloride	32	79—81° (749)	1.4059
Butyryl	164—165 (754)	45	12.36, 12.41	12.67	47.72, 47.78	48.00	Butyryl chloride	42	101—102 (754)	1.4118
Isobutyryl	158—159 (751)	52	12.45, 12.49	12.67	48.12, 48.17	48.00	Isobutyryl chloride	34	91—93 (751)	1.4085
Valeryl	70—71 (10)	55	11.80, 11.85	11.92	45.24, 45.29	45.15	Valeric anhydride	38	106—107 (10)	—
Isovaleryl	169—170 (747)	60	11.78, 11.83	11.92	45.25, 45.29	45.15	Isovaleryl chloride	28	114—115 (747)	1.4147
Trimethylacetyl	159—161 (750)	75	11.79, 11.86	11.92	45.22, 45.30	45.15	Trimethylacetyl chloride	17	105—106 (750)	—
Caproyl	65—66 (2)	66	11.13, 11.19	11.25	42.71, 42.77	42.62	Caproic anhydride	21	105—107 (2)	—
Capryl	109—110 (13)	86	9.98, 10.33	10.11	38.42, 38.48	38.31	—	—	—	—

*Literature data [3]: b.p. 130° (760 mm).
**The undistilled preparation was analyzed.

of absolute ether in a three-necked 500-ml flask fitted with stirrer, reflux condenser, and dropping funnel. The mixture was heated for 18—20 hr on a water bath, cooled, and poured in small portions with vigorous stirring into iced water acidified with hydrochloric acid. The ethereal layer was separated and the aqueous layer was extracted with ether. The combined ether extracts were washed with water, sodium carbonate, and again with water, and dried with potassium carbonate. After the ether had been driven off, the residue was fractionated to give the tertiary alcohol and the tetraalkylsilane. The latter was redistilled over sodium.

1. Methyldiethylcarbinol and tetraethylsilane. From 12.2 g magnesium, 54.5 g ethyl bromide, and 9.7 g acetoxytrichlorosilane was obtained: a) 4.2 g (82%) of methyldiethylcarbinol.

B.p. 120—121° (744 mm), n_D^{20} 1.4202, d_4^{20} 0.8297, MR_D 31.17. $C_6H_{14}O$. Calculated 31.44.

Literature data [5]: b.p. 122.8—123° (760 mm), n_D^{25} 1.4166, d_4^{25} 0.8233.

b) 5.2 g (72%) of tetraethylsilane.

B.p. 152—153° (744 mm), n_D^{20} 1.4272, d_4^{20} 0.7648.

Literature data [6]: b.p. 153.7° (760 mm), n_D^{20} 1.4267, d_4^{20} 0.7662.

2. Diethylbutylcarbinol and tetraethylsilane. From 12.2 g magnesium, 54.5 g ethyl bromide, and 11.8 g valeryloxytrichlorosilane was obtained: a) 5.75 g (80%) of diethylbutylcarbinol.

B.p. 69—70° (10 mm), n_D^{20} 1.4369, d_4^{20} 0.8381, MR_D 45.11 $C_9H_{20}O$. Calculated: 45.29.

Literature data [7]: b.p. 76.5—77.5° (15 mm) n_D^{20} 1.4362, d_4^{20} 0.8393.

b) 5.1 g (71%) of tetraethylsilane.

B.p. 151.5—152.5° (739 mm), n_D^{20} 1.4271, d_4^{20} 0.7650.

3. Diethylphenylcarbinol and tetraethylsilane. From 12.2 g magnesium, 54.6 g ethyl bromide, and 12.8 g benzoyloxytrichlorosilane was obtained: a) 6.7 g (82%) of diethylphenylcarbinol.

B.p. 105—106° (10 mm), n_D^{20} 1.5186, d_4^{20} 0.9825, MR_D 50.66. $C_{11}H_{16}OF_2$. Calculated: 50.92.

Literature data [8]: b.p. 111—113° (15 mm), n_D^{20} 1.5182, d_4^{20} 0.9831.

b) 3.8 g (53%) of tetraethylsilane.

B.p. 151.5—152.5° (740 mm), n_D^{20} 1.4272, d_4^{20} 0.7647.

4. Methyldipropylcarbinol and tetrapropylsilane. From 12.2 g magnesium, 61.5 g propyl bromide, and 9.7 g acetoxytrichlorosilane was obtained: a) 5.8 g (89%) of methyldipropylcarbinol.

B.p. 70—72° (10 mm), n_D^{20} 1.4275, d_4^{20} 0.8227, MR_D 40.66. $C_8H_{18}O$. Calculated: 40.67.

Literature data [9]: b.p. 159.5—160.5°, d_4^{20} 0.82357.

b) 7.8 g (78%) of tetrapropylsilane.

B.p. 88—89° (10 mm), n_D^{20} 1.4379, d_4^{20} 0.7847.

Literature data [10]: b.p. 90—91.5° (13 mm), n_D^{20} 1.4370, d_4^{20} 0.7838.

5. Methyldibutylcarbinol and tetrabutylsilane. From 12.2 g magnesium, 68.5 g butylbromide, and 9.7 g acetoxytrichlorosilane was obtained: a) 6.2 g (78%) of methyldibutylcarbinol.

B.p. 80—81° (9 mm), n_D^{20} 1.4352, d_4^{20} 0.8305, MR_D 49.74, $C_{10}H_{22}O$. Calculated: 49.90.

Literature data [7]: b.p. 91.4—92.4° (15 mm), n_D^{20} 1.4341, d_4^{20} 0.8290.

b) 10.2 g (79%) of tetrabutylsilane.

B.p. 114—116° (9 mm), n_D^{20} 1.4452, d_4^{20} 0.8011.

Literature data [10]: b.p. 105.5—108.8° (5 mm), n_D^{20} 1.4462, d_4^{20} 0.8005.

6. Dibutylheptylcarbinol and tetrabutylsilane. From 12.2 g magnesium, 68.5 g butyl bromide,and 13.9 g caproyloxytrichlorosilane was obtained: a) 9.0 g (74%) of dibutylheptylcarbinol.

B.p. 142—144° (10 mm), n_D^{20} 1.4515, d_4^{20} 0.8408, MR_D 77.71. $C_{16}H_{34}O$. Calculated: 77.61.

Literature data [11]: b.p. 131—135° (5 mm), n_D^{20} 1.4512, d_4^{20} 0.8415.

b) 9.7 g (76%) of tetrabutylsilane.

B.p. 115—117° (10 mm), n_D^{20} 1.4453, d_4^{20} 0.8009.

SUMMARY

1. The action of excess of silicon tetrachloride on monobasic organic acids of the aliphatic series leads to acyloxytrichlorosilanes.

2. The acyloxyoxytrichlorosilanes formed by aliphatic organic acids are easily disproportionated to tetra-acyloxysilanes and silicon tetrachloride. The tendency to disproportionate decreases with increasing number of carbon atoms in the straight chain of an organic acid and also with increased branching of acids with an iso structure.

3. Ethyl alcohol acts on acyloxytrichlorosilanes at -30° and displaces the organic acid.

4. Reaction of an acyloxytrichlorosilane with an acid other than that entering into its composition leads to formation of mixed anhydrides formed by silicic acid with two different organic acids.

5. Organomagnesium compounds act on acyloxytrichlorosilanes similarly to tetraacyloxysilanes, to form tertiary alcohols and tetraalkylsilanes.

LITERATURE CITED

[1] Yu. K. Yur'ev and Z. V. Belyakova, J. Gen. Chem. 28, 1755 (1958).*

[2] Yu. K. Yur'ev, Z. V. Belyakova,and V. P. Volkov, J. Gen. Chem. 29, 1463 (1959).*

[3] G. Goubeau and R. Mundiel, Z. allg. anorg. Ch. 272, 313 (1953).

[4] Yu. K. Yur'ev and Z. V. Belyakova, J. Gen. Chem 29, 1972 (1959).*

[5] J. Norris and F. Cortese, J. Am. Chem. Soc. 49, 2645 (1927).

[6] S. Tannenbaum, S. Kaye,and L. Lewenz, J. Am. Chem. Soc. 75, 3753 (1953).

[7] F. Whitmore and H. Woodburn, J. Am. Chem. Soc. 55, 361 (1933).

[8] A. de Coster, Bull. Acad. Belg. (5), 11, 661 (1925); Zbl. 1926, I, 3146.

[9] A. Gortaloff and A. Sautreff, J. pr. Ch. (2), 33, 203 (1886).

[10] A. D. Petrov and E. A. Chernyshev, Bull. Acad. Sci. Azerbaijan SSR 1953, 39; Ref. Zhur. Khim. 1954, 23354.

[11] A. D. Petrov and D. N. Andreev, J. Gen. Chem. 7, 570 (1937).

*Original Russian pagination. See C. B. Translation.

UNSATURATED DERIVATIVES OF THIOPHENE

I. THIENYL VINYL KETONE AND ITS PROPERTIES

N. I. Putokhin and V. N. Ivanova

Kuibyshev Industrial Institute

During our work in the thiophene field we undertook a study of monomers containing a thiophene ring which have not yet been reported in the literature. Here we describe our synthesis of thienyl vinyl ketone and its properties.

It was originally planned to synthesize thienyl vinyl ketone from allyl alcohol via dibromopropionyl chloride and dibromopropiothienone. However, the yield of dibromopropiothienone was insignificant (8—10%) and great difficulties were attached to the removal of bromine. We therefore made use of the method [1] based on decompositon of the tertiary amine with steam.

$$(C_4H_3SCOCH_2CH_2)_3N \cdot HCl \longrightarrow 3C_4H_3SCO-CH=CH_2 + NH_4Cl$$

The amine was synthesized in the form of the hydrochloride by the Mannich reaction [2] from acetothienone, formaldehyde and ammonium chloride. It was found that attainment of a maximum yield necessitated an aceto-thieneone: formaldehyde: ammonium chloride ratio of 3:45:1. Acetothienone was prepared by Gol'dfarb's method [3].

Thienyl vinyl ketone is a mobile, light-yellow oil with a pungent odor, easily soluble in benzene, less soluble in ether and alcohol. Yield up to 50% of the theoretical. Its structure was confirmed by determination of the sulfur content and by preparation and analysis of the bromide and semicarbazone, as well as by the ease of polymerization.

EXPERIMENTAL

Tri(propiothienone)amine hydrochloride. 11.25 g of acetothienone, 1.58 g of ammonium chloride, and 7.35 ml (about 2/3 of the required quantity) of 33.5% formaldehyde were placed in a 100-ml round-bottomed flask to which a reflux condenser was attached. The flask was heated one hour on a water bath, another 3.9 ml formaldehyde solution was added, and heating was continued for 2 hr. An oil accumulated at the bottom of the flask and gradually crystallized on standing in the cold. After 48 hr the filtrate was drained on a Nutsch and the crystals were washed with alcohol. They were further purified by trituration with alcohol and were then suction-filtered once again and dried in the air. Yield 6.73 g (48%). An additional 0.9 g of crystals was collected from the mother liquor after prolonged standing. The total yield of amine hydrochloride was up to 55%. White crystals readily soluble in hot water, poorly soluble in alcohol. M.p. 174-175° after recrystallization from aqueous alcohol.

Found %: N 3.36, 2.85; S 20.28, 20.24. $C_{21}H_{22}O_3NClS_3$. Calculated %: N 2.99; S 20.53.

Thienyl vinyl ketone was prepared by steam distillation of 4 g of tri(propiothienone)amine hydrochloride. The distillate was twice extracted with ether; the ether solution was dried with calcium chloride. Removal of the ether left a mobile, yellow oil with a pungent and irritating odor.

d^{18} 1.1755, n_D^{18} 1.5870, MR_D 38.908; calc. 39.002.

Found %: S 22.93. C_7H_6OS. Calculated %: S 23.18.

Preliminary experiments on the polymerization of thienyl vinyl ketone. Heating of 1.2 g of the ketone in a sealed test tube (length 110 mm, diameter 10 mm) at 50—60° for 35 hr gave a poorly mobile oil that could be

drawn into a thread. Rise of temperature to 100° speeded up polymerization (10 hr) and gave a transparent, yellow, horny product.

Semicarbazone. 0.46 g of thienyl vinyl ketone was dissolved in 10 ml of alcohol in a 100-ml round-bottomed flask,and a solution of 1 g of semicarabazide and 0.9 g of sodium acetate in 10 ml of water was added. The flask was connected to a reflux condenser and the contents were gently boiled for 2.5 hr on an air bath. The solution became transparent and yellow, and after a few hours fine yellow crystals were deposited. These were filtered, washed with water and dried. Yield 0.32 g (50%). M.p. 135—137°.

Found %: N 21.75, 22.0.$C_8H_9ON_3S$. Calculated %: N 21.53.

Bromide. Bromine was added dropwise from a capillary pipet to a solution of 0.25 g of thienyl vinyl ketone in 10 ml of ether in a 50 ml beaker until the solution was no longer decolorized. The mass was left in the air until the ether had evaporated. The bromide was quickly crystallized. Yield 0.36 g (66%).

Found %: Br 53.45 (Stepanov method). $C_7H_6OSBr_2$. Calculated %: Br 53.62.

SUMMARY

Tri(propiothienone)amine hydrochloride was synthesized. Thienyl vinyl ketone was synthesized and characterized.

LITERATURE CITED

[1] H. Schäfer and B. Tollens, Ber. 29, 2181 (1906); C. Mannich and S. M. Abdulbach, Ber. 68, 113 (1935).

[2] R. Adams, Collection: Organic Reactions I [Russian translation] (1948) p. 399.
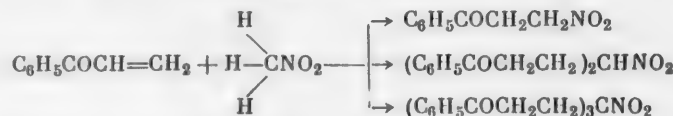
[3] Ya. L. Gol'dfarb, J. Russ. Chem. Soc. 62, 1073 (1930).

THE ADDITION OF NITROALKANES TO PHENYL VINYL KETONE

S. S. Novikov, I. S. Korsakova, and N. N. Bulatova

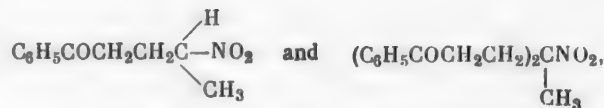Moscow Institute of Engineering Physics

In continuation of our study of the addition of nitroalkanes to compounds containing an activated double bond, we set out to clarify the laws of addition to phenyl vinyl ketone of various nitroalkanes differing from one another in respect to the number of nitro groups and labile hydrogen atoms. It could be assumed that addition would depend to a marked extent on the acidity of the starting nitroalkanes and that the presence of several labile hydrogen atoms would cause the reaction to take one of the following possible courses:

$$C_6H_5COCH{=}CH_2 + H{-}\overset{\displaystyle H}{\underset{\displaystyle H}{C}}NO_2 \longrightarrow \begin{cases} C_6H_5COCH_2CH_2NO_2 \\ (C_6H_5COCH_2CH_2)_2CHNO_2 \\ (C_6H_5COCH_2CH_2)_3CNO_2 \end{cases}$$

The addition of nitromethane, nitroethane, 2-nitropropane, and 1,1-dinitroethane to various α, β-unsaturated ketones has been described in the literature [1—9]; these studies do not, however, provide the answer to our problem.

Experiments undertaken with phenyl vinyl ketone showed that trinitromethane, dinitromethane, and 1,1-dinitroethane smoothly add on to phenyl vinyl ketone at room temperature. Addition proceeds with especial ease in the case of trinitromethane. In the case of 1,1-dinitroethane the addition of sodium ethoxide as catalyst to the reaction mixture shortens the reaction period to 2 hr (instead of 24).

Dinitromethane and nitroethane, each containing two labile hydrogen atoms, can combine with one or two molecules of ketone to form a monoketone and a diketone respectively. At room temperature, for example, dinitromethane easily reacts with phenyl vinyl ketone to form $C_6H_5COCH_2CH_2CH(NO_2)_2$ with a dinitromethane ketone molar ratio of 1:1, and with formation of the diketone $(C_6H_5COCH_2)_2C(NO_2)_2$ with a dinitromethane ketone ratio of 1:2. Using the same molar ratios, two products of addition of nitroethane to phenyl vinyl ketone could similarly be obtained:

$$C_6H_5COCH_2CH_2\overset{\displaystyle H}{\underset{\displaystyle CH_3}{C}}{-}NO_2 \quad \text{and} \quad (C_6H_5COCH_2CH_2)_2\underset{\displaystyle CH_3}{C}NO_2,$$

although catalytic quantities of sodium ethoxide were present in this case.

Nitromethane easily reacts with phenyl vinyl ketone at room temperature in presence of sodium ethoxide to give a product of addition at two labile hydrogen atoms, i.e., the diketone $(C_6H_5COCH_2CH_2)_2CHNO_2$ with a nitromethane ketone molar ratio of 1 : 1. The product of addition of nitromethane to phenyl vinyl ketone at one labile hydrogen atom $C_6H_5COCH_2CH_2CH_2NO_2$ could also be prepared but only by using a 10-fold excess of nitromethane.

No special experiments aimed at clarifying the mechanism of addition were carried out in this work. However, the isolation of products of addition at one labile hydrogen atom of a nitroalkane (dinitromethane, nitroethane, or nitromethane) shows that addition is apparently a stepwise process. With nitroethane, for example, it may be represented thus:

Products of Addition of Nitroalkanes to Phenyl Vinyl Ketone

| Nitroalkane | Reactants taken | | | Reaction period (hr) | Substances obtained | Yield (%) | Melting point | Empirical formula | % C | | % H | | % N | |
	molar ratio	quantity (g) of nitroalkane	of phenyl vinyl ketone						found	calc.	found	calc.	found	calc.
Nitromethane*	1 : 1	1.2	2.5	4	4-Nitro-1,7-diphenyl-1,7-heptanedione	52	130—131°	$C_{19}H_{19}O_4N$	70.06, 70.03	70.15	5.94, 6.03	5.84	4.55, 4.42	4.30
Nitromethane	10 : 1			20	1-Nitro-4-phenyl-4-butanone	36	51—52	$C_{10}H_{11}O_3N$	61.97, 62.22	62.17	5.85, 5.85	5.69	7.21, 7.37	7.25
Nitroethane*	1 : 1	1.4	2	18	4-Nitro-1-phenyl-1-pentanone	58	54—55	$C_{11}H_{13}O_3N$	63.66, 63.92	63.77	6.23, 6.33	6.23	6.75, 6.64	6.76
Nitroethane*	1 : 2	0.8	2.6	3	4-Nitro-1,7-diphenylheptane-1,7-dione	95	145—146	$C_{20}H_{21}O_4N$	70.80, 71.00	70.79	6.42, 6.36	6.19	3.96, 4.15	4.13
Dinitromethane*	1 : 1	2.7	3.3	5	1,1-Dinitro-4-phenyl-4-butanone	49	77—78	$C_{10}H_{10}O_5N_2$	50.67, 50.54	50.41	4.31, 4.41	4.67	11.45, 11.63	11.76
Dinitromethane*	1 : 2	1.1	2.9	3	4,4-Dinitro-1,7-diphenylheptane-1,7-dione	48	135—136	$C_{19}H_{18}O_6N_2$	61.00, 61.20	61.62	5.09, 4.94	4.86	8.02	7.57
1,1-Dinitroethane**	1 : 1	3.5	3.3	20	2,2-Dinitro-5-phenyl-5-pentanone	64	101—102	$C_{11}H_{12}O_5N_2$	52.76, 52.80	52.38	4.79, 4.86	4.76	11.04, 11.94	11.10
Trinitromethane**	1 : 1	3.2	2.6	3	1,1,1-Trinitro-4-phenyl-4-butanone	70	80—81	$C_{10}H_9O_7N_3$	42.44, 42.32	42.40	3.32, 3.16	3.18	14.45, 14.32	14.84

* Prepared in a methanol medium.

** Prepared in an ethanol medium.

$$C_6H_5COCH=CH_2 + CH_2NO_2 \longrightarrow C_6H_5COCH_2CH_2CHNO_2 \xrightarrow{CH_2CH_2NO_2}$$
$$\underset{CH_3}{|} \qquad\qquad\qquad \underset{CH_3}{|}$$

$$\longrightarrow C_6H_5COCH_2CH_2\overset{\overset{\textstyle HO_2}{|}}{\underset{\underset{\textstyle CH_3}{|}}{C}}CH_2CH_2COC_6H_5.$$
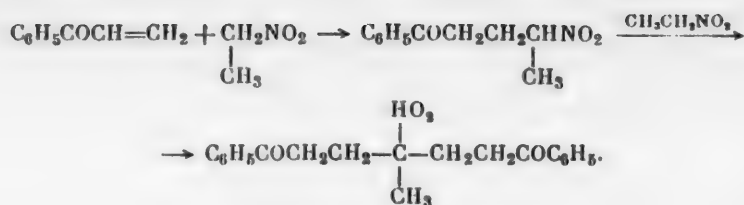
EXPERIMENTAL

Phenyl vinyl ketone was prepared by thermal decomposition in vacuo of β-dimethylaminopropiophenol hydrochloride [10] with b.p. 83—84° (7.5 mm); literature: b.p. 74—76° (4 mm) [10] and 72—73° (3 mm) [11].

Addition of nitroalkanes to phenyl vinyl ketone was performed in a flask fitted with mechanical stirrer, condenser, thermometer, and dropping funnel. About 0.1 g of hydroquinone was added to the reaction mixture as a precaution against polymerization. An ethanol solution of sodium ethoxide (a few drops) was used as catalyst.

The reaction conditions and the properties of the prepared ketones are presented in the table.

SUMMARY

1. The addition of nitroalkanes to phenyl vinyl ketone was investigated.

2. It was shown that addition of nitroalkanes to the α, β-unsaturated ketone in question under our chosen conditions proceeds easily with formation of the corresponding addition products. Sodium ethoxide as catalyst considerably accelerates the reaction.

3. It was shown that nitroalkanes containing more than one labile hydrogen atom give products of addition at two labile hydrogen atoms when the nitroalkane and ketone are taken in the appropriate molar ratios. Such "double" addition products were obtained with nitromethane, nitroethane, and dinitromethane.

LITERATURE CITED

[1] E. P. Kohler, J. Am. Chem Soc. 38, 899 (1916).

[2] E. P. Kohler, J. Am. Chem. Soc. 46, 503 (1924).

[3] E. P. Kohler, L. J. Smith, J. Am. Chem Soc. 45, 2944 (1923).

[4] E. P. Kohler, C. S. Deway, J. Am. Chem. Soc. 46, 1274 (1924).

[5] D. E. Worral, C. J. Bradway, J. Am. Chem. Soc. 52, 1607 (1935).

[6] T. C. Klotzel, J. Am. Chem. Soc. 69, 227 (1947).

[7] H. Schechter, L. Zeldin, J. Am. Chem. Soc. 73, 1276 (1951).

[8] BIOS Final Report N 709.

[9] S. S. Novikov, I. S. Korsakova, M.D. Yatskovskaya, Proc. Acad. Sci. USSR 118, 954 (1958).*

[10] A. Ya. Yakubovich, V. V. Razumovskii, and I. N. Belyaev, J. Gen. Chem. 28, 680 (1958).

[11] W. G. Joung, J. D. Roberts, J. Am. Chem. Soc. 58, 651 (1949).

---

* Original Russian pagination. See C. B. Translation.

THERMAL BREAKDOWN OF TETRAETHYLLEAD AND HEXAETHYLDIPLUMBANE IN THE LIQUID PHASE
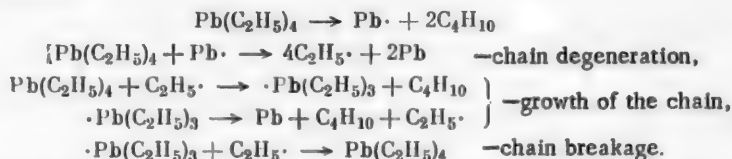
G. A. Razuvaev, N. S. Vyazankin, and N. N. Vyshinskii

Gorkii State University

In 1929 Paneth and Hofeditz [1] demonstrated the formation of free alkyl radicals by thermal decomposition of tetraalkyl derivatives of lead in the gas phase. According to Paneth [2] the breakdown of compounds of this type, and in particular of tetraethyllead, can be represented by the equation

$$(C_2H_5)_4Pb \longrightarrow Pb + 4C_2H_5 \cdot \qquad\qquad (I)$$

The above investigations were followed by widespread utilization of thermal breakdown of tetraethyllead for study of the properties and transformation products of ethyl radicals in the gas [3, 4] and liquid [5, 6] phases. On the other hand, very little work had been published about the actual mechanism of breakdown of tetraalkyl compounds of lead, and the actual process of thermal breakdown has remained obscure.

We know that lead forms a series of less alkylated derivatives (tri- and dialkyllead) which can play an extremely important part in the reaction. The kinetics of thermal breakdown of tetraethyllead in the gas phase have been studied by Leermakers [7], and in the liquid phase by Berlin [8]. According to the former author, thermal breakdown is a homogeneous monomolecular reaction with $E = 36.9$ kcal/mole. Berlin reports more complex kinetic relations in the breakdown of tetraethyllead in the liquid phase. This author suggests an autocatalytic process with $E = 33.7$ kcal/mole. He proposed the following chain mechanism on the basis of the character of the kinetic curves and of some indirect observations:

$$Pb(C_2H_5)_4 \longrightarrow Pb\cdot + 2C_4H_{10}$$
$$[Pb(C_2H_5)_4 + Pb\cdot \longrightarrow 4C_2H_5\cdot + 2Pb \qquad \text{—chain degeneration,}$$
$$Pb(C_2H_5)_4 + C_2H_5\cdot \longrightarrow \cdot Pb(C_2H_5)_3 + C_4H_{10} \ \Big\}$$
$$\cdot Pb(C_2H_5)_3 \longrightarrow Pb + C_4H_{10} + C_2H_5\cdot \ \Big\} \text{—growth of the chain,}$$
$$\cdot Pb(C_2H_5)_3 + C_2H_5\cdot \longrightarrow Pb(C_2H_5)_4 \qquad \text{—chain breakage.}$$

This scheme, however, is speculative in character since the author had no direct evidence of its validity. This defect has also been noted by the author himself.

Less study has been devoted to the thermal decomposition of hexaethyldiplumbane. Only one type of breakdown of compounds R_6Pb_2 (hexaethyldiplumbane in particular) has been described [9, 10]:

$$2(C_2H_5)_6Pb_2 \longrightarrow 3(C_2H_5)_4Pb + Pb. \qquad\qquad (II)$$

Joint decomposition of hexamethyl- and hexaethyldiplumbane [11] proceeds without evolution of gases, which is likewise consistent with equation (II). The possibility of decomposition of hexaethyldiplumbane by any other mechanism is not reported in the literature. As far as we know, no study has been made of the kinetics of this process.

It is therefore evident that quite inadequate investigation has been made of the liquid-phase thermal decomposition of tetraethyl lead and hexaethyldiplumbane. This is also true of the majority of other classes of organometallic compounds. At the same time this process is undoubtedly of theoretical interest, and also of practical interest in the case of tetraethyl lead.

A. Procedure. Thermal decomposition was investigated in the absence of atmospheric oxygen. Air was removed from the tetraethyllead and hexaethyldiplumbane and ampoules were filled in the apparatus sketched (Fig. 1).

The organolead compound was put into section A and the apparatus was connected to a vacuum pump. The material in A was frozen with liquid nitrogen in the case of tetraethyllead and its solutions in isooctane and of solutions of hexaethyldiplumbane in n-heptane, and the whole of the system was exhausted to high vacuum. With tap C closed, the solution was then thawed and again frozen. Tap C was opened and the apparatus was again exhausted; the set of ampoules was then sealed off at the zone D. The material in section A was uniformly filled into the small ampoules and the lengths of tubing connecting them to the large ampoule were sealed off. Freezing was not practised in the case of hexaethyldiplumbane which has an extremely low vapor tension.
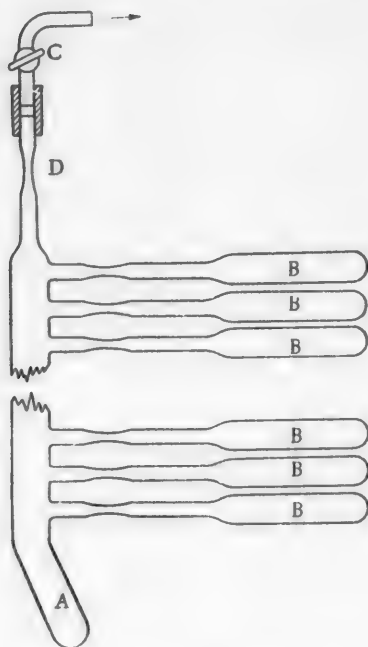
The amount of substance in ampoules B was determined by weighing. The filled ampoules were kept for a certain period in a thermostat; their contents were then frozen with liquid nitrogen. After the ampoules had been opened and thawed, the reaction mixture was filtered from metallic lead and analyzed by spectroscopy and polarography. The metallic lead was repeatedly washed with ether and analyzed by the molybdate method.

A manometric method of investigation was also used in addition to the above procedure. For this purpose the ampoule A was attached to a mercury manometer C (Fig. 2).

During study of the kinetics of the initial period of decomposition, the free space of the ampoule was small (2.5—4.0 ml); during study of the extensive transformations of hexaethyldiplumbane the free space was made equal to 300 ml. In both of the cases the ampoule was evacuated (~1 mm mercury column) after charging with hexaethyldiplumbane, and the ampoule was sealed. During an experiment the apparatus was completely immersed in the thermostatting liquid.

Apart from observations of the vapor pressure rise in the ampoule, far-reaching transformations of hexaethyldiplumbane were studied by determination (at the end of an experiment) of the quantity of precipitated lead and of the composition of the gas mixture.

Fig. 1. Apparatus for removing free oxygen from substances.

B. Purification and synthesis of starting compounds. Tetraethyllead. A technical product was purified by distillation with steam and subsequent treatment with sulfuric acid [12], water, sodium hydroxide solution, and water. The dried material was repeatedly fractionated in vacuo in a hydrogen stream:

B.p. 82° (13 mm), n_D^{20} 1.5214.

Literature [10]: b.p. 78° (10 mm), n_D^{20} 1.5195.

The lead content of the preparation was 99.81% of the theoretical; the content of hexaethyldiplumbane was less than 0.05% (determined by polarography). The spectrophotometric curve of absorption of tetraethyllead (D = f (λ), d = 0.020 mm) is shown in Fig. 3, curve 1.

Hexaethyldiplumbane. It was synthesized by a modification of Hein's method [13]. 7 g of triethyllead chloride was dissolved in 50 ml of 2.5 N potassium hydroxide solution. To the solution was added 1.5 g of aluminum powder. The mixture was held for 20 hr at 15—18°, after which the hexaethyldiplumbane was separated from the aqueous layer and quickly filtered through a paper filter into section A of the apparatus shown in Fig. 1. Here it was freed of oxygen of the air and dried with sodium sulfate in the course of 24 hr. The dried material was transferred to the small ampoules B. This preparation of hexaethyldiplumbane was stable for 5—6 days in the absence of atmospheric oxygen and light. Yield, quantitative; d_4^{20} 1.9473. The lead content of the preparation was 98.4% of the theoretical.

The spectrophotometric curve of optical density versus wavelength of light absorbed at a layer thickness of 0.020 mm is plotted in Fig. 3, curve 3. This shows that the absorption curve of hexaethyldiplumbane is considerably shifted towards the long-wave region so that the compound has a yellow color.

Solution of diethyllead in hexaethyldiplumbane. • This was prepared on the same lines as the previous product. 7.1 g of dichlorodiethyllead was dissolved in 50 ml of 2.5 N potassium hydroxide solution. To the solution was added 1.5—2.0 g of aluminum powder without external cooling of the reaction vessel with water. After 5—7 minutes of violent reaction, the mixture was quickly transferred to a separating funnel externally cooled with ice-water. The bright-red liquid was separated from the water layer and filtered into an ampoule in which a high vacuum was quickly established. Yield 27.8 g of the theoretical, d_4^{20} 1.9653.

Found %: Pb 71.48, 71.77. $(C_2H_5)_6Pb_2$. Calculated %: Pb 70.39. $(C_2H_5)_2Pb$. Pb 78.09.

The optical data of the synthesized product differ from those of hexaethyldiplumbane; it is characterized by still greater light absorption in the blue, dark-blue, and violet regions of the spectrum (Fig. 3,6); this behavior determines its characteristic color.
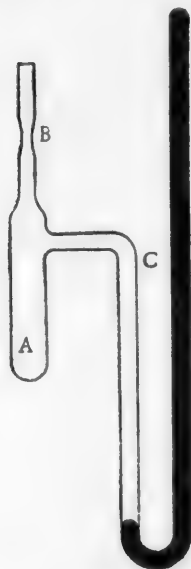

Fig. 2. Apparatus for investigation of the kinetics of thermal decomposition of hexaethyldiplumbane by the manometric method.
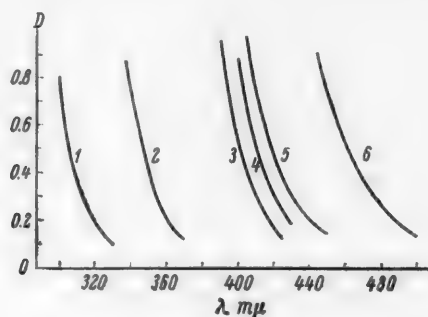

Fig. 3. Spectrophotometric absorption curves.

1) tetraethyllead; 2) tetraethyllead which had been partially decomposed (25 min at 115°); 3) hexaethyldiplumbane; 4) n-hexa-ethyldiplumbane after partial decomposition (50 min at 85°); 5) the same after 10 min at 105°; 6) solution of diethyllead in hexa-ethyldiplumbane.

The product is stable at the temperature of liquid nitrogen. At room temperature, in the absence of oxygen of the air, metallic lead is deposited and gaseous products are evolved within 10—15 min after synthesis (or unfreezing); in the course of the breakdown the physical properties— in particular the spectrophotometric characteristics — gradually approach those of pure hexaethyldiplumbane. The result is that after 24 hr (from the start of decomposition) the substance is transformed into a liquid hardly distinguishable from hexaethyldiplumbane.

DISCUSSION OF RESULTS

Kinetics of breakdown of tetraethyllead and of its solutions in isooctane. Data for the kinetics of thermal breakdown of tetraethyllead in the absence of solvents are plotted in Fig. 4. The progress of decomposition was followed by determination of the metallic lead formed.

Figure 4 shows that the decomposition of tetraethyllead at the start of the process can formally be regarded as a zero order reaction. Only after fairly considerable transformation (30—35%) is a fall in reaction rate observed, and this can be attributed both to a fall in the quantity of tetraethyllead undergoing decomposition and to a considerable accumulation of the product of decomposition.

*R. F. Galiulina took part in the work.

We can therefore calculate the velocity constants of the reaction with the help of the equation $K = 1/t(C_0 - C)$, where $\underline{t}$ is the time in seconds and $C_0 - C$ is the quantity (moles) of tetraethyllead decomposed after time $\underline{t}$.

The dependence of log K on 1/T is plotted in Fig. 5. The activation energy of the over-all process, on the basis of Fig. 5, is 35.4 kcal/mole.
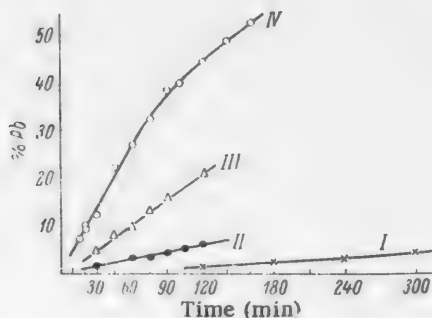

Fig. 4. Kinetic curves of thermal breakdown of tetraethyllead at various temperatures.
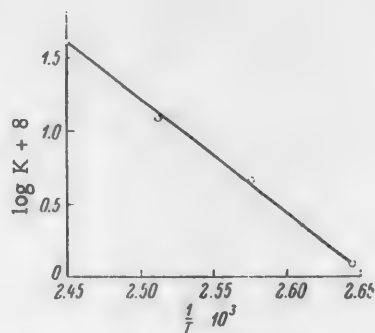
I) 105°, II) 115°, III) 125°, IV) 135°.

Fig. 5. Log K as a function of 1/T.

As noted above, simultaneous investigation of the liquid fraction was carried out while the quantity of precipitated lead was being determined. One of the products of decomposition of tetraethyllead was identified as hexaethyldiplumbane.

Since the formation of hexaethyldiplumbane has not been reported in the literature, the presence of this compound in the reaction mixture was confirmed by three independent methods: by the spectroscopic method of N. K. Rudnevskii and N. N. Vyshinskii; by the polarographic method [14]; and by titration of the hexaethyldiplumbane with a solution of potassium permanganate in acetone under conditions such that tetraethyllead is not oxidized.

Figure 6 contains plots of the amount of hexaethyldiplumbane in the residues of undecomposed tetraethyllead. These results are based on spectral and polarographic analyses. •

The two methods give a similar picture of the change of concentration of hexaethyldiplumbane in the course of breakdown of tetraethyllead. At the same time the spectral method gives results which are systematically too low. It will be shown below that this deviation may be attributed to the presence in the reaction mixture of small quantities of diethyllead side by side with the hexaethyldiplumbane. A comparison of the curves in Figs. 4 and 6 justifies the conclusion that hexaethyldiplumbane is an intermediate and not a secondary product of decomposition.

The initial phases of thermal breakdown of solutions of tetraethyllead in isooctane can similarly be regarded as a zero order reaction (Fig. 7) if the progress of the reaction is checked by determinations of the metallic lead precipitated. The dependence of log K on 1/T for this case is plotted in Fig. 8. On the basis of these results the velocity constant of the reaction can be expressed by

$$K = 2.43 \cdot 10^{12} e^{\dfrac{-35200}{RT}} .$$

Kinetics of decomposition of hexaethyldiplumbane and its solutions in n-heptane. As already noted, the mechanism described in the literature for the breakdown of hexaethyldiplumbane (II) does not allow for the formation of gaseous products. We were unable to confirm this mechanism in our experiments with hexaethyldiplumbane or its solutions in n-heptane. In both of the cases decomposition followed another route:

$$(C_2H_5)_6Pb_2 \longrightarrow (C_2H_5)_4Pb + Pb + 2C_2H_5 . \tag{III}$$

•L. N. Vertyulina determined hexaethyldiplumbane in tetraethyllead by the polarographic method.

Decomposition of hexaethyldiplumbane in the absence of solvent, for example, was invariably accompanied by formation of a gas; this behavior enabled us to check the progress of decomposition by the manometric method (Fig. 9). It was established that separation of 1 g-atom of metallic lead is accompanied by formation of 1.60 — 1.75 mole of a gaseous mixture of the following percentage composition: ethane 54.02, 55.68; ethylene 43.05, 41.63; butane 2.93, 2.69.

The gas was analyzed by gas chromatography. The composition of the gas mixture is evidence that breakdown of hexaethyldiplumbane is accompanied by release of ethyl radicals whose products of disproportionation are ethane and ethylene. Further experiments are needed in order to account for the ethane content being a little higher than that of ethylene.

Less characteristic of the process in question is the dimerization of ethyl radicals to n-butane.

· Finally, it is evident from the ratio of the quantities of metallic lead and gases that gas formation is not a secondary step; consequently the hexaethyldiplumbane is decomposed in accordance with equation (III).

Equation (III) is also valid for the decomposition of hexaethyldiplumbane when in solution in n-heptane (Fig. 10). In this case, the process was followed by two methods: by spectroscopic determination of the percent transformation of hexaethyldiplumbane (curves I—VI) and by chemical determination of the metallic lead (curves 1—6). It

Fig. 6. Change of concentration of hexaethyldiplumbane in tetraethyllead (in wt.%) during thermal decomposition of tetraethyllead at various temperatures.

1) 105°; 2 and 6) 115°; 3) 125°; 4 and 5) 135°. Curves 1—4 are plotted from polarographic data, curves 5 and 6 are based on spectroscopic data.

is evident from Fig. 10 that the hexaethyldiplumbane is substantially all converted into tetraethyllead at the point when 50% of the lead has separated as metal. This observation is consistent with equation (III) and contradicts equation (II). It does not follow from what has been said, however, that we deny the possibility of breakdown of hexaethyldiplumbane in accordance with equation (II). The linear character of the kinetic curves (Fig. 10) suggests a zero order reaction for the decomposition of hexaethyldiplumbane, in particular, in the initial stages. Since the breakdown was checked by two independent methods, the velocity constant could be calculated by two routes, and consequently the activation energy of the over-all reaction likewise. Two forms of the depencence of log K on 1/T are therefore plotted in Fig. 11.
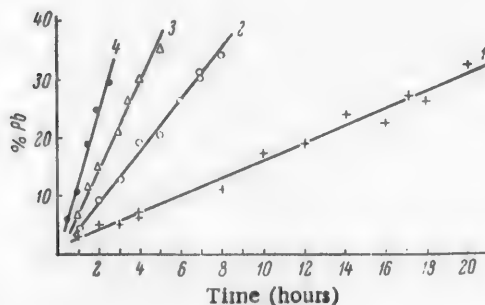
Fig. 7. Kinetic curves of thermal breakdown of a 0.3232 molar solution of tetraethyllead in isooctane at various temperatures.

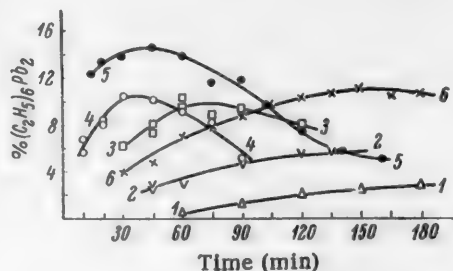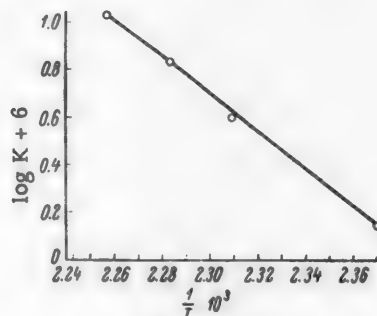1) 148.7°; 2) 160°, 3) 165°, 4) 170°.

Fig. 8. Log K as a function of 1/T.

On the basis of the data obtained, we can express the velocity constant by the expression $K = 5.89 \times 10^{10} \times e^{-\frac{11500}{RT}}$

if the calculation is based on the spectroscopic investigation of the lowering of the concentration of hexaethyl-diplumbane in the course of decomposition, and by $K = 2.44 \times 10^{10} \times e^{\frac{2800}{RT}}$ if K is calculated on the basis of the speed of accumulation of metallic lead.

Since we had established that hexaethyldiplumbane is formed in the course of breakdown of tetraethyllead, it seemed probable that hexaethyldiplumbane in turn could break down, with intermediate formation of less alkylated organolead compounds. In order to test this hypothesis, we studied the kinetics of thermal decomposition of hexa-ethyldiplumbane in the absence of solvents in the 70—125° temperature range (Figs. 9 and 12). At the same time the change in optical density of the hexaethyldiplumbane during its decomposition was measured at 70, 85, and 105° (Fig. 13). The data obtained from these experiments led to the conclusion that one of the intermediate products of decomposition of hexaethyldiplumbane is diethyllead. One fact in support of this conclusion is the red color, characteristic of diethyllead, which is developed on partial decomposition of hexaethyldiplumbane. We made a similar observation when tetraethyllead was partially de-composed (in this case the reaction mixture acquired the lemon-yellow color of hexaethyldiplumbane). The spectral data also lend support to the theory of intermediate forma-tion of diethyllead.

Figure 3 shows the spectrophotometric absorption curves of pure tetraethyllead, of hexaethyldiplumbane, and of the solution of diethyllead in hexaethyldiplumbane that we prepared. On the same diagram are also plotted the ab-sorption curves of tetraethyllead and hexaethyldiplumbane which had been subjected to partial thermal decomposition.

We see from the diagram that, after thermal break-down tetraethyllead has a greater optical density in the corresponding spectral region than the starting product, and a lower optical density than hexaethyldiplumbane. We can therefore conclude that hexaethyldiplumbane is one of the products of thermal decomposition of tetraethyllead. It has already been noted that this conclusion was supported by chemical and polarographic evidence.

We also see from Fig. 3 that hexaethyldiplumbane, after partial decomposition, occupies in respect to its spectro-photometric characteristics a position intermediate between pure hexaethyldiplumbane and the solution of diethyllead in hexaethyldiplumbane that we synthesized. It is logical to attribute this to the formation of a compound with a stronger light absorption (in this instance diethyllead) during thermal decomposition of hexaethyldiplumbane. Indeed, if decomposition had occurred without intermediate formation of diethyllead, then in the initial stages of decomposition we should have observed not an increase but a decrease of optical density due to dilution of the hexaethyldiplumbane by the tetraethyllead formed. In spite of numerous attempts, we did not succeed in synthesizing pure diethyllead. It was therefore impossible to develop a method of quantitative determination of this substance in solutions. At the same time, the change of its amount in course of breakdown of hexaethyldiplumbane can be qualitatively evaluated from the change of optical density of the reaction medium (Fig. 13).
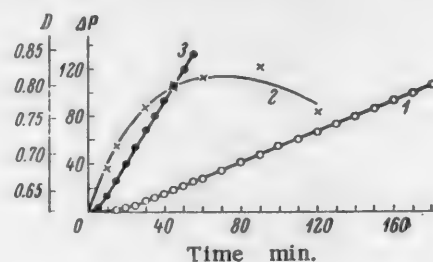
Fig. 9. Kinetics of initial decomposi-tion of hexaethyldiplumbane (up to the stage of 0.5% transformation):

1) rise of pressure at 70°; 2) rise of pressure at 85°; 3) change of optical density (D) of hexaethyldiplumbane, λ 400 mμ, d 0.020 mm at 70°.
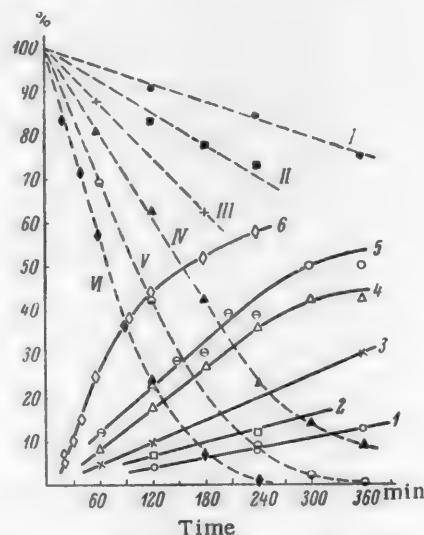
Fig. 10. Kinetics of thermal decomposi-tion of a 0.1385-molar solution of hexa-ethyldiplumbane in n-heptane.
1 and I 105°; 2 and II 110°; 3 and III 115°; 4 and IV 120°; 5 and V 125°; 6 and VI 130°; I—VI are % transformations of $(C_2H_5)_4Pb_2$; 1—6 are % Pb separated.
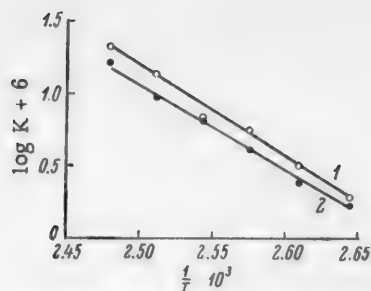
Fig. 11. Log K versus 1/T.

1) based on spectral analysis.
2) based on chemical analysis.

Fig. 12. Kinetic curves of the decomposition of hexaethyldiplumbane at various temperatures.

1) 95°, 2) 105°, 3) 115°, 4) 125°.

The curves of Fig. 13 are consequently consistent with the data represented in Fig. 6 for the change of concentration of hexaethyldiplumbane during thermal decomposition of tetraethyllead.

The similarity in character of the curves (presence of maxima, shift of the maxima to the coordinate axes with rise of temperature, etc.) is additional evidence of the correctness of our ideas about intermediate formation of diethyllead during breakdown of hexaethyldiplumbane.

The possibility of qualitative evaluation of the buildup of diethyllead by spectral analysis enables us to draw certain conclusions about the processes taking place in the initial stage of decomposition of hexaethyldiplumbane.

As we see from Fig. 9, the decomposition of this product at certain temperatures, in particular at 70° (curve 1), has a well-marked induction period. Curve 2 shows, moreover, that during the induction period there is a considerable increase in the optical density of hexaethyldiplumbane, and consequently an increase in its content of diethyllead.

Fig. 13. Curves of change of optical density (D) of hexaethyldiplumbane during its decomposition (wavelength 400 mμ, thickness of absorbing layer 0.020 mm).

1) at 70°, 2) at 85°, 3) at 105°.

It can therefore be expected that the addition of diethyllead to hexaethyldiplumbane would shorten the induction period. This assumption is supported by the fact that our synthesized solutions of diethyllead in hexaethyldiplumbane are extremely unstable, whereas pure hexaethyldiplumbane does not break down at room temperature in the course of several days.

The experimental material set forth in this this paper shows that the breakdown of tetraethyllead and of hexaethyldiplumbane has a complex mechanism.

On the other hand we must agree with Berlin [8] in his statement that the sharp change in velocity of decomposition of tetraethyllead after trace quantities of a series of other substances had been added testifies to a chain reaction.

Since one of the intermediate products of breakdown of tetraethyllead is hexaethyldiplumbane, we must assume that the primary breakdown step is detachment of one C_2H_5 group with formation of a $(C_2H_5)_3Pb$ radical.

$$(C_2H_5)_4Pb \longrightarrow (C_2H_5)_3Pb \cdot + C_2H_5 \cdot$$

$$\text{(IV)}$$

In this case hexaethyldiplumbane can be formed by growing chains:

$$(C_2H_5)_3Pb \cdot + (C_2H_5)_4Pb \longrightarrow (C_2H_5)_3Pb - Pb(C_2H_5)_3 + C_2H_5 \cdot$$

$$\text{(V)}$$

and by chain breakage: $$2(C_2H_5)_3Pb \cdot \longrightarrow (C_2H_5)_3Pb-Pb(C_2H_5)_3 \tag{VI}$$

In the preceding section it was shown that breakdown of hexaethyldiplumbane goes in accordance with equation (III), i.e. with release of gases.

On the other hand, we have a sufficient amount of experimental material in support of the fact that diethyllead is an intermediate in the breakdown of hexaethyldiplumbane.

Consequently, the breakdown of hexaethyldiplumbane is more correctly represented not by equation (III) but by a combination of the following equations:

$$(C_2H_5)_3Pb-Pb(C_2H_5)_3 \longrightarrow (C_2H_5)_4Pb + Pb(C_2H_5)_2 \tag{VII}$$

$$Pb(C_2H_5)_2 \longrightarrow Pb + 2C_2H_5 \cdot \tag{VIII}$$

Since a comprehensive study of the subsequent fate of the ethyl radicals or a study of the processes bound up with the appearance of a fresh phase (metallic lead) was outside the scope of the present work, the authors do not by any means claim to have given the full details of the thermal decomposition of tetraethyllead and hexaethyldiplumbane by a chain mechanism. However, such schemes should evidently take equations (IV) to (VIII) into consideration. In other words, we can assume gradual detachment of ethyl radicals from the decomposing molecule with intermediate formation of hexaethyldiplumbane and diethyllead (compounds in which the lead is not in its maximum valency form).

The foregoing investigation and the literature data also show that tetraethyllead, hexaethyldiplumbane, and diethyllead are capable of undergoing reciprocal transformations.

This behavior is largely responsible for the very great difficulties of isolation of the pure substances.

It was shown above that repeated fractionation does not free tetraethyllead of traces of hexaethyldiplumbane, and this is not surprising, since the former changes into the latter at higher temperatures. Even greater difficulties arise in attempts to prepare pure hexaethyldiplumbane or to estimate its purity.

We know that hexaethyldiplumbane [14] and triethyllead chloride [15] are reduced by nascent hydrogen. On the other hand, Hein's [13] synthesis of hexaethyldiplumbane takes place in a reducing medium, due to which a secondary product is usually metallic lead. The possibility of formation of other reduction products, in particular diethyllead, cannot be ruled out. This would account for the reddish tint of hexaethyldiplumbane at the start of synthesis and for the high optical density. On heating (Hein's procedure) or on maintenance at room temperature, metallic lead comes down and the optical density falls. Consequently the hexaethyldiplumbane synthesized by Hein's method evidently always contains some tetraethyllead and diethyllead, and at present there is no sort of criterion for the accurate determination of the composition of this mixture.

Similar difficulties arise in the study of solutions of diethyllead in hexaethyldiplumbane.

SUMMARY

1. The kinetics of liquid-phase thermal decomposition of tetraethyllead and of its solutions in isooctane were studied in the 105—170° temperature range.

2. It was shown that tetraethyllead decomposes with gradual detachment of ethyl radicals from the decomposing molecule and with intermediate formation of less alkylated compounds—hexaethyldiplumbane and diethyllead.

3. A study was made of the kinetics of thermal decomposition of hexaethyldiplumbane in n-heptane and also in the absence of solvent.

4. It was established that apart from the disproportionation reaction noted in the literature:

$$2(C_2H_5)_6Pb_2 \longrightarrow 3(C_2H_5)_4Pb + Pb,$$

hexaethyldiplumbane also undergoes the following characteristic breakdown reaction:

$$(C_2H_5)_6Pb_2 \longrightarrow (C_2H_5)_4Pb + Pb + 2C_2H_5 \cdot$$

The gaseous products were investigated and some facts were adduced that demonstrated the formation of diethyllead as an intermediate in this reaction.

5. A procedure was developed for estimation of the change of concentrations of intermediate products (hexaethyldiplumbane and diethyllead) during liquid-phase decomposition of tetraethyllead and hexaethyldiplumbane.

LITERATURE CITED

[1] F. Paneth and W. Hofeditz, Ber. 62, 1335 (1929).

[2] F. Paneth and W. Lautsch, Ber. 64, 2702 (1931).

[3] H. S. Taylor and W. H. Jones, J. Am. Chem. Soc. 52, 1111 (1930).

[4] R. N. Meinert, J. Am. Chem. Soc. 55, 979 (1933).

[5] P. L. Cramer, J. Am. Chem. Soc. 56, 1234 (1934).

[6] P. L. Cramer, J. Am. Chem. Soc. 60, 1406 (1938).

[7] J. A. Leermakers, J. Am. Chem. Soc. 55, 4508 (1933).

[8] L. E. Berlin, Trans. NII (State Chem. Press, Moscow) 1, 35 (1958).

[9] H. Gilman and J. C. Bailie, J. Am. Chem. Soc. 61, 731 (1939).

[10] R. W. Leeper, L. Summers and H. Gilman, Chem. Revs. 54, 101 (1954).

[11] G. Calingaert, H. Soroos and H. Shapiro, J. Am. Chem. Soc. 64, 462 (1942).

[12] G. Calingaert, Chem. Revs. 2, 43 (1925).

[13] F. Hein and A. Klein, Ber. 71, 2381 (1938).

[14] L. A. Korshunov and L. N. Bertyulina, Works on Chemistry and Chemical Technology [in Russian] (Gorkii), (in the press).
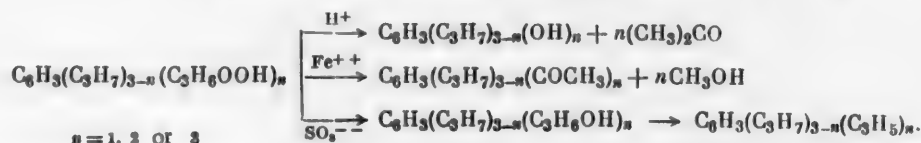
[15] L. Riccoboni, Gazz. 72, 47 (1942).

LIQUID-PHASE AUTOOXIDATION OF TRIISOPROPYLBENZENES

R. N. Volkov and S. V. Zavgorodnii

Voronezh State University

Triisopropylbenzene hydroperoxides are good initiators of emulsion polymerization [1] and, like cumene hydroperoxide, can be converted to phenols, ketones, alcohols, and propenyl derivatives according to the scheme:

$$C_6H_3(C_3H_7)_{3-n}(C_3H_6OOH)_n \begin{cases} \xrightarrow{H+} C_6H_3(C_3H_7)_{3-n}(OH)_n + n(CH_3)_2CO \\ \xrightarrow{Fe++} C_6H_3(C_3H_7)_{3-n}(COCH_3)_n + nCH_3OH \\ \xrightarrow{SO_4^=} C_6H_3(C_3H_7)_{3-n}(C_3H_6OH)_n \longrightarrow C_6H_3(C_3H_7)_{3-n}(C_3H_5)_n. \end{cases}$$

$$n = 1, 2 \text{ or } 3$$

There is only one original investigation [2] on the synthesis of the stated hydroperoxides, although triisopropyl-benzenes are obtained in good yields by alkylating diisopropylbenzenes— byproducts of cumene production.

The autoxidation of 1,2,4-triisopropylbenzene (I) and 1,3,5-triisopropylbenzene (II) was studied in the present work. It was found that (I) is oxidized by atmospheric oxygen, in the presence of manganese resinate and soda at 110°, to a maximum concentration of hydroperoxide in the solution equal to 53%. In this case only the isolated isopropyl group is oxidized, whereas the other two groups, which are adjacent to each other, hinder each other and practically are not oxidized. As a result, only monohydroperoxide (A) is formed.
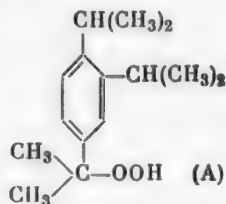
For these reasons we were unable to oxidize 1,2,4,5-tetraisopropylbenzene to the corresponding hydroperoxide.

The autooxidation of (II) was studied by Seidel et al. [2]. The authors found that in the liquid phase in the presence of alkali, (II) is oxidized by atmospheric oxygen to the extent of 51% in 64 hours, whereas in emulsion form it is oxidized to the extent of 150-186% in 72 hours. By the extent of oxidation is meant the molar percentage of oxygen absorbed by the hydrocarbon.

We studied the autooxidation of (II) under different conditions. It was found that in the presence of manganese resinate and soda (II) is oxidized exceptionally vigorously by atmospheric air. The average initial rate amounts to 20-30% hydroperoxides per hour. Thus in the oxidation of 1 mole of (II) in the presence of 15 mg of manganese resinate and 3 g of soda at 110°, with an air feed rate of 1.5 liters/ minute, the extent of autooxidation of the first 3 hours is 93%, and after 10 hours, 196%; such a rate of autoxidation is not recorded for a single alkylbenzene. In this case a mixture of 1,3,5-triisopropylbenzene mono-, di-, and trihydroperoxides is formed according to the scheme:

$$(CH_3)_2CH-\underset{\underset{\displaystyle \overset{CH_3}{\underset{CH_3}{C}}-OOH}{|}}{\overset{\displaystyle CH(CH_3)_2}{\bigcirc}}-CH(CH_3)_2 \xrightarrow{O_2} (CH_3)_2CH-\underset{\underset{\displaystyle \overset{CH_3}{\underset{CH_3}{C}}-OOH}{|}}{\overset{\displaystyle \overset{\displaystyle CH_3}{\underset{CH_3}{C}}-OOH}{\bigcirc}}-CH(CH_3)_2 \xrightarrow{O_2}$$

$$\xrightarrow{} (CH_3)_2CH-\underset{}{\bigcirc}-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{C}}-OOH \xrightarrow{O_2} HOO-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{C}}-\bigcirc-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{C}}-OOH$$

A peroxide and tertiary alcohols are obtained as by-products.

Course of autooxidation of 1,3,5-triiso-propylbenzene. I) Twenty mg/mole of manganese resinate, 5 g/mole of soda, air feed rate 2 liters/minute, temperature 120°; II) 5 mg/mole of manganese resinate, 3 g/mole of soda, air feed rate 1-1.5 liters/minute, temperature 110°; III) 3 mg/mole of manganese resinate, 2 g/mole of soda, air feed rate 1-1.5 liters/minute, temperature 110° (in the segment forming a discontinuity in the curve, air was supplied at a rate of 0.2-0.3 liter/minute).

For an extent of oxidation up to 150% there are practically no byproducts in the reaction mass (values of the extent of oxidation, determined iodometrically and by the amount of tertiary alcohols formed, agree closely). From a mixture in which the extent of oxidation of (II) is 145%, di- and trihydroperoxides may be isolated; the residue, which has a hydroperoxide concentration of 79%, is reoxidized. In this case the extent of oxidation reaches 101, 122, and 147% after 2, 4, and 7 hours, respectively. To obtain increased yields of the trihydroperoxide, it is expedient to interrupt the autooxidation when its extent is 150-160%, to isolate the trihydroperoxide from the reaction mass, and to subject the remaining mixture again to autooxidation.

The course of autooxidation of (II) for the most characteristic cases is shown in the diagram.

EXPERIMENTAL

1,2,4-Triisopropylbenzene (I) was prepared by alkylating p-diisopropylbenzene with propylene in the presence of $H_3PO_4 \cdot BF_3$ [3]. Before oxidation it was treated with concentrated sulfuric acid, passed through "KIL" clay, washed with water and alkali, and distilled over sodium; b. p. 238-239°, n_D^{20} 1.4914, d_4^{20} 0.8618.

1,3,5-Triisopropylbenzene (II) was prepared in practically quantitative yield by alkylating diisopropylbenzene with propylene in the presence of 10 mol % of aluminum chloride at 65-70°. The product, distilled through a 25-plate column, had high purity; it did not contain the 1,2,4-isomer, since on nitration it was converted to 2-nitro-1,3,5-triisopropylbenzene, m. p. 75°, corresponding to literature data [4], in 98% yield (1,2,4-triisopropylbenzene gives a liquid mononitro derivative). The product having b. p. 236-236.5°, n_D^{20} 1.4880, d_4^{20} 0.8550, was used without further purification.

Autooxidation of (I). Into a glass column with a sealed-in air-jet (Schott filter), provided with an efficient coil condenser and situated in an oil thermostat, were placed (I) and either soda or sodium hydroxide. The mixture was heated to a certain temperature, and air was passed through at a given rate until 1-6% of the hydroperoxide was formed; manganese resinate was then added to the hot mixture and autooxidation continued under these conditions until the hydroperoxide concentration decreased. The course of the oxidation was followed iodometrically.

Data of the most characteristic experiments are given in Table 1.

TABLE 1

Autooxidation of 1,2,4-Triisopropylbenzene

Taken per mole of hydrocarbon		Air feed rate (liters/hr)	Temp.	Oxidation in the presence of of soda		Final	
manganese resinate (in mg)	soda (in g)			time (hr)	yield of hydroperoxide (in %)	time (hours)	optimum yield of hydroperoxide (in %)
6	1.1*	12	85°	4	1	20	24
6	1.0	20	100	15	6	25	49
6	1.0**	30	110	10	4	27	48
10	1.2	60	110	3	1	11	50
10	3.0	60	110	10	2	40	32
10	4.0	100	110	—	—	12	38
15	2.0	120	110	4	2	13	53

*Sodium hydroxide was used.

**The hydrocarbon was not treated with sulfuric acid.

TABLE 2

Autooxidation of 1,3,5-Triisopropylbenzene

Taken per mole of hydrocarbon		Air feed rate (liters/hr)	Initial		Final	
manganese resinate (in mg)	soda (in g)		extent of oxidation (in %)	time (hr)	extent of oxidation (in %)	time (hr)
15*	5	90	6	5	189	14
20**	5	120	99	3	161	8
5	3	60—90	27	1.5	202	12
3	2	60—90	24	2	145	10.5
10	2	90	65	3	178	9
15	3	60—90	93	3	196	10

*The manganese resinate was added after oxidation for 5 hours with soda alone.

**The experiment was carried out at 120°.

Conversion of 1,2,4-triisopropylbenzene hydroperoxide (III). Cleavage of (III) into 3,4-diisopropylacetophenone (IV). Twenty-five g of 50% 1,2,4-triisopropylbenzene hydroperoxide (III) was stirred with an equivalent quantity of 0.5 N $FeSO_4$ solution for 3 hours at room temperature and 2 hours at 100°. After appropriate treatment and distillation there was obtained 7.1 g, or 64.8% of the theoretical yield of 3,4-diisopropylacetophenone (IV).

B. p. 105-106.5° (2.5 mm), n_D^{20} 1.5169, d_4^{20} 0.9561, MR_D 64.7; Calc. 63.3.

Ketone (IV) gave the iodoform reaction; the semicarbazone, recrystallized from alcohol, melted with partial decomposition at 178-179°. This product was obtained along with 3,4-diisopropylbenzoic acid (V) by oxidizing (I) with 15% nitric acid. Ketone (IV) was oxidized with 3% alkaline permanganate solution at 30-40° to a mixture of diisopropylbenzoic (V) and diisopropylphenylglyoxylic (VI) acids. The latter acid was converted to acid (V) by hydrogen peroxide.

M. p. 147.3-147.8° (corr.) (from alcohol).

Found %: C 75.91; H. 8.87. M. 206.7 (reckoned on the silver salt). $C_{13}H_{18}O_2$. Calculated %: C 75.68; H. 8.80. M. 206.3.

Substance (V) was 3,4-diisopropylbenzoic acid, since the other isomers, which could have been obtained by oxidation of (I), melt much lower (71 and 108°).

For a more rigorous proof of the structure of (V), the acid was converted by decarboxylation to o-diisopropylbenzene, and the latter was oxidized to phthalic acid (anhydride melting point 130°).

Reduction of (III). To 20 g of 48% hydroperoxide (III) were added 30 ml of 30% sodium hydroxide solution, 5 g of zinc dust, and 20 ml of alcohol. The mixture was refluxed until the (III) was fully decomposed, and then treated with ether; the ethereal extract was washed with water, dried, and distilled. There was obtained 10.7 g (96%) of 1-(α-hydroxyisopropyl) - 3,4-diisopropylbenzene (VII).

B.p. 111° (3 mm), m.p. 44-45° (from petroleum ether), n_D^{20} 1.5070 d_4^{20} 0.9344.

Found %: C 81.87; H 10.73. M. 216.9. $C_{15}H_{24}O$. Calculated %: C 81.75; H 10.98. M. 220.3.

3,4-Diisopropyl-α-methylstyrene was obtained by distilling (VII) over sodium bisulfate.

B. p. 253-255° (corr.), 100-102° (3 mm), n_D^{20} 1.5162, d_4^{20} 0.8963, MR_D 68.39; Calc. 67.50.

Acid cleavage of (III). Better conditions, under which 3,4-diisopropylphenol (VIII) was obtained in 76% yield and acetone in 62% yield, are described in the following. Thirty g of 40% hydroperoxide (III) was added to a mixture of 1 g of 30% hydrogen peroxide and 1 ml of concentrated sulfuric acid at 0°, with good stirring, and the mixture was further stirred for 3 hours at 15-20°. Then 4-6 drops more of concentrated sulfuric acid were added and the temperature raised to 50°. The sulfuric acid was neutralized with soda, the acetone (1.9 g) driven off, and the (VIII) extracted from the residue with dilute alkali, in the form of the phenoxide; the latter was washed with benzene and treated with hydrochloric acid; phenol (VIII) was extracted with ether and distilled. Yield 6.85 g. 3,4-Diisopropylphenoxyacetic acid melted at 97-98°. M 237.5 . $C_{14}H_{20}O_3$. Calculated M 236.3.

The autoxidation of (II) was carried out like that of (I), but (in all experiments except the first) the manganese resinate and soda were added directly to the hydrocarbon. Data of the most characteristic experiments are given in Table 2.

Separation of the mixture of 1,3,5-triisopropylbenzene mono-, di-, and trihydroperoxides. After preliminary washing with soda the reaction mass was added to twice its volume of boiling benzene, stirred until the hydroperoxides were almost completely dissolved (a peroxide soluble with difficulty in hot benzene remained), and left in the dark for 12-16 hours. The crystals which had separated were filtered out by suction and recrystallized from benzene. In this case 1,3,5-triisopropylbenzene trihydroperoxide (IX) was isolated, whereas 1,3,5-triisopropylbenzene dihydroperoxide (X) remained in the mother liquor. For more complete extraction of (IX) the mother liquor was treated several times with 5-10% sodium hydroxide solution. The hydroperoxide salt solution was washed with benzene and decomposed with carbon dioxide. The crystals were filtered out by suction and recrystallized. The operation was repeated until the extraction of (IX) was complete. Thus 1 mole of (II), oxidized to 161%, gave 9.8% of (IX) and 6% of peroxide (XI). A mixture in which the extent of oxidation was 202%, gave 19.9% of (IX) and 11% of (XI) on extraction (yields reckoned on the hydrocarbon).

Trihydroperoxide (IX) consisted of fine white crystals with m. p. 139-140° (from benzene). On reduction with sodium sulfite,(IX) was quantitatively converted to 1,3,5-tri- (α-hydroxyisopropyl) benzene, m. p. 150-151.5°. After removal of (IX), dihydroperoxide (X) was isolated from the benzene mother liquor by dilution with petroleum ether, and also through the sodium salt; m.p. 97-98° (from a benzene-petroleum ether mixture). On reduction with sodium sulfite (X) gave 3,5-di- (α-hydroxyisopropyl) cumene, m. p. 118-120° (from benzene).

1,3,5-Triisopropylbenzene monohydroperoxide (XII) was reduced to 3,5-diisopropyl-α-hydroxycumene, m. p. 42-44° (after repeated distillation in vacuo). The melting points of the stated compounds corresponded to literature data [2].

Peroxide (XI) was formed as a by-product when (II) was extensively oxidized; it probably has the following structure.
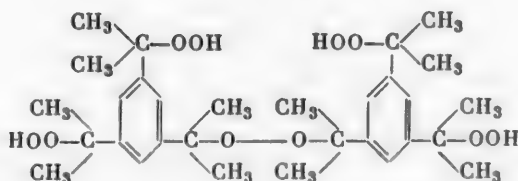
It consisted of fine, white crystals,which gradually decomposed about 180° without melting.

Found %: O_{act} 13.49 (Iodometrically). M 541. $C_{30}H_{46}O_{10}$. Calculated %: O_{act} 14.11. M 566.4.

On reduction (XI) gave 1,3,5-tri-(α-hydroxyisopropyl) benzene in quantitative yield.

It was found, by reduction of a mixture of 1,3,5-triisopropylbenzene hydroperoxides to carbinols by means of an excess of sodium sulfite, that when the extent of oxidation was 202.5%, mono-, di-, and trihydroperoxides, and also peroxides were present in the mixture in the molar ratio 1:2.13:0.95:0.53.

SUMMARY

The autooxidation of 1,2,4- and 1,3,5-triisopropylbenzenes by atmospheric air in the presence of manganese resinate and alkaline admixtures was studied. It was shown that on oxidation 1,2,4-triisopropylbenzene forms a monohydroperoxide, whereas 1,3,5-triisopropylbenzene gives a mixture of mono-, di-, and trihydroperoxides. Conditions were found under which 1,3,5-triisopropylbenzene is oxidized at an initial average rate of 30% per hour to an extent of 200%.

1,2,4-Triisopropylbenzene hydroperoxide was converted to 3,4-diisopropylacetophenone, 3,4-diisopropyl-benzoic acid, and 3,4-diisopropylbenzene.

LITERATURE CITED

[1] G. S. Uitbi,* Synthetic Rubber. GKhI, 257 (1957).

[2] F. Seidel, M. Schulze, and H. Baltz, J. prakt. Chem. 5, 278 (1956).

[3] S. V. Zavgorodnii and R. N. Volkov, J. Gen. Chem. 29, 1447 (1959). **

[4] Newton, J. Am. Chem. Soc. 65, 2434 (1943).

---

*Name not verified.

**Original Russian pagination. See C. B. Translation.

INVESTIGATION IN THE FIELD OF THE REACTION OF C-ACYLATION OF HETEROCYCLIC KETOENOLS

I. 3-ACYL-4-HYDROXYCARBO STYRILS

N. S. Vul'fson and R. B. Zhurin

State Scientific Research Institute of Organic Intermediated and Dyes

The possibility of C-acylation of 4-hydroxycoumarin by aliphatic acids in the presence of phosphorus oxychloride to form the corresponding 3-acyl-4-hydroxycoumarins was shown several years ago in the works of Klosa [1]. We attempted to extend this reaction to the 4-hydroxycarbostyril series in order to prepare 3-acyl-4-hydroxycarbostyrils. A number of the latter were obtained earlier in low yields from 4-hydroxycarbostyril by the Friedel-Crafts reaction and by the Fries rearrangement of certain 4-acylhydrocarbostyrils [2]. Further, two more methods for the preparation of 3-acetyl-4-hydroxycarbostyril are described: cyclization of methyl N-acetoacetylanthranilate and the reaction of aniline with acetylmalonic ester [3]. Similar methods were used to prepare 1-methyl-3-acyl-4-hydroxycarbostyrils.

We found that 4-hydroxycarbostyril and 1-methyl-4-hydroxycarbostyril react with acetic acid in the presence of phosphorus oxychloride to give only the corresponding 4-acetoxy derivatives; i.e., O-acylation took place in the given case, in contrast to the case of 4-hydroxycoumarin, where C-acylation occurred.

We succeeded in preparing a number of 3-acyl-4-hydroxycarbostyrils by acylating 4-hydroxycarbostyril with aliphatic acids, using polyphosphoric acid, which recently has come into ever-increasing use for analogous reactions [4], as a condensing agent.

The 3-acyl-4-hydroxycarbostyrils obtained were colorless substances which crystallized from alcohol in the form of needles and gave a characteristic yellow-orange coloration with ferric chloride; they were very soluble in dilute alkalis and were liberated unchanged from the alkaline solutions by acids.

EXPERIMENTAL

4-Hydroxycarbostyril was prepared by the cyclization of methyl N-acetylanthranilate according to the cited method [5] in 35% yield. M.p. 350—354°; literature data [6]: m.p. 352—354°.

1-Methyl-4-hydroxycarbostyril was prepared by the cited method [7] in 55% yield. M. p. 250—260°; literature data [7]: m.p. 252—262°.

4-Acetoxycarbostyril. Five g of 4-hydroxycarbostyril, 10 ml of glacial acetic acid, and 8 ml of phosphorus oxychloride were gradually heated to 100° during 30 minutes and stirred at this temperature for 35 minutes. On cooling, the thickened mass was poured into ice; the precipitate formed was filtered out, washed with water, dried, and recrystallized from alcohol. Yield 2.2 g (35%). Colorless needles with m.p. 217—219°. A mixture test with the substance obtained by the cited method [5] gave no melting-point depression.

1-Methyl-4-aceotxycarbostyril. A mixture of 2 g of 1-methyl-4-hydroxycarbostyril, 11 ml of glacial acetic acid, and 4 ml of phosphorus oxychloride was boiled for 25 minutes. On cooling, the mobile upper layer was decanted and the tarry lower layer decomposed with ice; the precipitate, which separated from the lower layer, was filtered out, washed with water, and dried. There was obtained 1.1 g of the original 1-methyl-4-hydroxycarbostyril. A white substance separated from the decanted upper layer on standing, which was filtered out, washed with water

dried, and recrystallized from alcohol. There was obtained 0.7 g (62.5%, reckoned on the 1-methyl-4-hydroxy-carbostyril taken into the reaction) of colorless needles with m.p. 142.5–143.5°. A mixture test with the substance obtained by the cited method [2] gave no melting-point depression.

3-Acetyl-4-hydroxycarbostyril. Two g of 4-hydroxycarbostyril, 10 ml of glacial acetic acid, and 50 ml of polyphosphoric acid(prepared by dissolving 100 g of phosphoric anhydride in 100 ml of 85% orthophosphoric acid) were stirred for 2.5 hours at 85–90°. The mass, while still hot, was poured into ice, and after a few hours the resulting precipitate was filtered out, washed with water, and dried. Yield 2.0 g (80%). After recrystallization from alcohol, 1.7 g of colorless needles with m.p. 255–257° was obtained. A mixture test with the substance obtained by the cited method [3] gave no melting-point depression.

Found %: C 65.12, 65.38; H 4.56, 4.60; N 6.96, 6.98. $C_{11}H_9O_3N$. Calculated %: C 65.02; H 4.43; N 6.89.

Similarly, 4-hydroxycarbostyril and the corresponding acids gave the following 3-acyl-4-hydroxycarbostyrils:

3-Propionyl-4-hydroxycarbostyril in 72% yield.

M.p. 224–225°; literature data [3]: m.p. 225–226°.

Found %: C 66.17, 66.28; H 4.95, 4.88; N 6.71, 6.88. $C_{12}H_{11}O_3N$. Calculated %: C 66.35; H 5.06; N 6.45.

3-Butyroyl-4-hydroxycarbostyril in 70% yield.

M.p. 217–219°; literature data [3]: m.p. 218–219°.

Found %: C 67.66, 67.72; H 5.57; 5.46; N 6.17, 6.34. $C_{13}H_{13}O_3N$. Calculated %: C 67.52; H 5.62; N 6.06.

3-Isovaleroyl-4-hydroxycarbostyril in 51% yield.

M.p. 197–198°; literature data [3]: m.p. 195–198°.

Found %: C 68.66, 68.75; H 6.32, 6.24; N 5.75, 5.84. $C_{14}H_{15}O_3N$. Calculated %: C 68.57; H 6.12; N 5.71.

3-Caproyl-4-hydroxycarbostyril in 48% yield.

M.p. 184–185°; literature data [3]: m.p. 183–184°.

Found %: C 69.58, 69.65; H 6.62, 6.71; N 5.19, 5.25. $C_{15}H_{17}O_3N$. Calculated %: C 69.49; H 6.56; N 5.40.

SUMMARY

On reaction of 4-hydroxycarbostyril with aliphatic acids in a polyphosphoric acid medium a number of the corresponding 3-acyl-4-hydroxycarbostyrils were obtained, while in the presence of phosphorus oxychloride only 4-acyloxy derivatives were formed.

LITERATURE CITED

[1] J. Klosa, Arch. Pharm. 288/60, 356 (1955); 289/61, 104, 143, 156 (1956).

[2] K. Tomita, J. Pharm. Soc. Japan 71, 1100 (1951); C. A. 46, 5044 (1952.

[3] R. N. Lacey, J. Chem. Soc. 1954, 850.

[4] K. Nakazawa et al, J. Pharm. Soc. Japan 74, 69, 495, 498, 836, 1254, 1256 (1954); Referat Zhur. Khim. 74884, 78106 (1956); S. Dev, J. Indian Chem. Soc. 33, 703 (1956).

[5] J. N. Ashley, W. H. Perkin and R. Robinson, J. Chem. Soc. 1930, 382.

[6] E. H. Huntress and J. Bornstein, J. Am. Chem. Soc. 71, 745 (1949).

[7] R. E. Lutz and J. F. Codington, J. Am. Chem. Soc. 68, 1810 (1946).

ON THE ACTION OF HALOGENS ON THE ETHYLENIC BOND OF o-CARBOXY-
AND o-CARBOXYDIMETHOXYBENZALBARBITURIC ACIDS

E. I. Chukhina

Second Moscow Medical Institute

The main purpose of this work was to study the action of the halogens chlorine, bromine and iodine on o-carboxy- and o-carboxydimethoxybenzalbarbituric acids. The original acids were obtained earlier by the condensation of o-formylbenzoic and opianic acids with barbituric acid in an aqueous medium [1].

Bromination and chlorination took place in dioxane medium at room temperature. Four halo derivatives of benzalbarbituric acids, (I), (II), (III), and (IV), containing one halogen atom in the molecule, were obtained (in yields over 90% when a 15—20% excess of bromine or a 50—60% excess of chlorine was used).
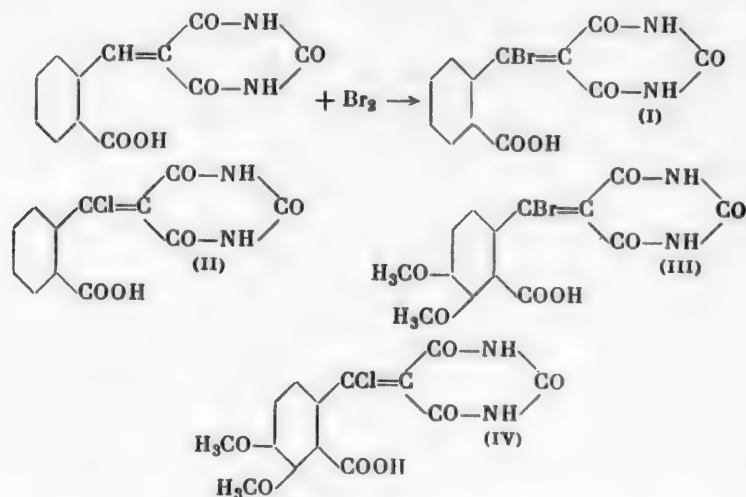
In order to prove the position of the halogen in benzalbarbituric acids, the reaction of debromination of bromo-o-carboxybenzalbarbituric acid by an excess of aniline in an alkaline medium [2] was investigated, and anil-o-formylbenzoic acid and a compound which was soluble in soda, corresponded on analysis to the formula of the ureide of anilinomalonic acid (V), and on alkaline hydrolysis was readily converted to anilinomalonic acid, • were isolated.

Thus the debromination of the bromo derivative of benzalbarbituric acid by aniline took place with cleavage of the ethylenic bond:
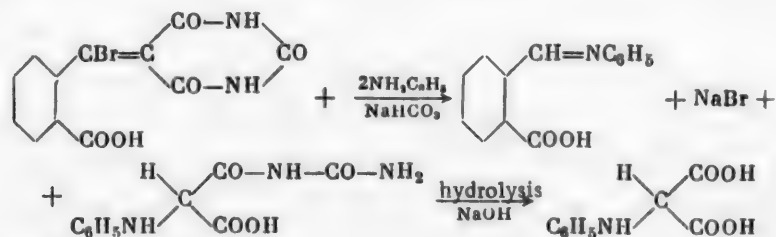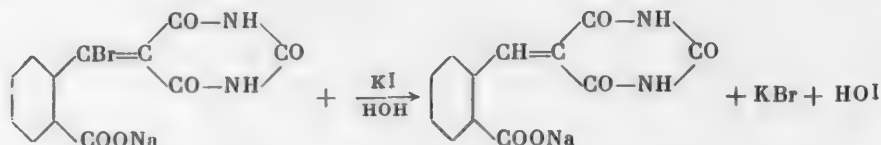

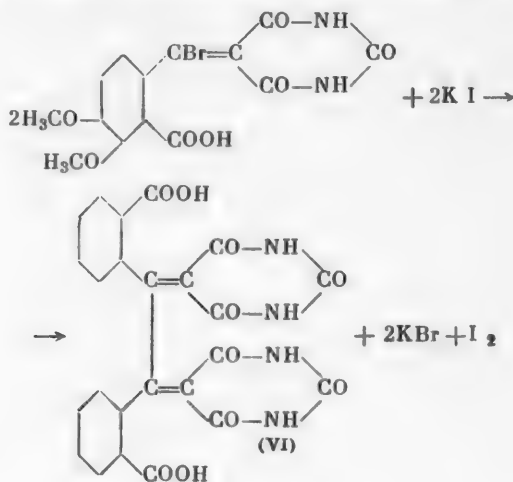
• Br^- ion was found in the aqueous solution.

On the basis of the debromination reaction, as well as analysis of the chlorine and bromine content, it could be concluded that under mild conditions chlorine and bromine replace hydrogen at the ethylenic bond but do not add to the latter. It was found that neutral iodine could not replace a hydrogen atom at the ethylenic bond.

On treatment of the bromo derivatives of benzalbarbituric acids with potassium iodide, debromination took place, but not iodination, even though bromine easily displaced iodine from potassium iodide.

In the reaction of potassium iodide with the sodium salt of the bromo derivative of benzalbarbituric acid, the free acid was isolated.

$$\underset{\text{COONa}}{\overset{\text{CBr=C}}{\bigcirc}}\overset{\text{CO—NH}}{\underset{\text{CO—NH}}{\diagdown}}\text{CO} + \frac{\text{KI}}{\text{HOH}} \longrightarrow \underset{\text{COONa}}{\overset{\text{CH=C}}{\bigcirc}}\overset{\text{CO—NH}}{\underset{\text{CO—NH}}{\diagdown}}\text{CO} + \text{KBr} + \text{HOI}$$

In the reaction of potassium iodide with the bromo derivative of o-carboxydimethoxybenzalbarbituric acid a substance was formed which was soluble in soda and slightly soluble in water, and did not melt at 300° or more. The elementary analysis corresponded to o-carboxydimethoxybenzalbarbituric acid. The substance was reduced by zinc in an acetic acid medium, a mixture of o-carboxydimethoxybenzal- and benzylbarbituric acids being formed. A substance with these properties was prepared from the bromo derivative of o-carboxydimethoxybenzal-barbituric acid by the Wurtz reaction (with zinc in an anhydrous alcohol or dioxane medium). On heating a mixture of the substances obtained in these experiments to 300° or more, no depression was observed. It was assumed that these compounds are dimers of o-carboxydimethoxybenzalbarbituric acid (VI). •

$$2\text{H}_3\text{CO}—\underset{\underset{\text{COOH}}{\text{H}_3\text{CO}}}{\overset{\text{CBr=C}}{\bigcirc}}\overset{\text{CO—NH}}{\underset{\text{CO—NH}}{\diagdown}}\text{CO} + 2\text{KI} \longrightarrow$$

$$\longrightarrow \quad (\text{VI}) \quad + 2\text{KBr} + \text{I}_2$$

EXPERIMENTAL

<u>Action of halogens on o-carboxy- and o-carboxydimethoxybenzalbarbituric acids:</u>

a) <u>Bromination.</u> To 9.9 g of o-carboxybenzalbarbituric acid mixed with about 30 ml of dioxane, 7.5 g of bromine was added dropwise, with continuous stirring. When the substance was almost completely dissolved in the dioxane, the solution was filtered and poured into ice water; 10.55 g of the bromo derivative was obtained from it, in the form of acicular crystals with m.p. 240—241° (dec. from 230°). • •

Found %: Br 23.60; N 8.20. $C_{12}H_7O_5N_2Br$. Calculated %: Br 23.60; N 8.26. Br 20.05; N 7.02.

From 4.1 g of o-carboxydimethoxybenzalbarbituric acid, 4.28 g of the bromo derivative was isolated in the form of acicular crystals with m.p. 207—208° (dec. from 130°).

Found %: Br 20.05; N 7.00. $C_{14}H_{11}O_7N_2Br$.

• Iodine was isolated from the aqueous solution.
• • The melting point was determined in an apparatus heated beforehand to 230°.

<u>Action of aniline on the bromo derivative of o-carboxybenzalbarbituric acid</u>. A 6.95 g quantity of the sodium salt of the bromo derivative of o-carboxybenzalbarbituric acid was heated in a water bath for 3.5 hours, with stirring, with 7.2 g of freshly-distilled aniline and 1.63 g of sodium bicarbonate dissolved in 7 ml of water. The solution was treated with ether and then acidified with acetic acid; 1.2 g of anil-o-formylbenzoic acid, m.p. 174—175° (from alcohol) was obtained.

Found %: N 6.29. $C_{14}H_{11}O_2N$. Calculated %: N 6.22.

A mixture test of this substance with anil-o-formylbenzoic acid prepared by the Racine method [3] gave no melting-point depression. After the filtrate was evaporated to about $\frac{2}{3}$ of its initial volume and reacidified with hydrochloric acid ($\underline{d}$ 1.17), about 1 g of the substance was isolated in the form of colorless plates (from water) with m.p. about 250° (dec.).

Found %: N 17.90. $C_{10}H_{11}O_4N_3$. Calculated %: N 17.72.

On alkaline hydrolysis this substance was converted to anilinomalonic acid.

b) <u>Chlorination</u>. Into a mixture of 2 g of o-carboxybenzalbarbituric acid and about 13 ml of dioxane,was passed the chlorine obtained from 0.75 g of potassium permanganate and 5 ml of hydrochloric acid ($\underline{d}$ 1.17). The excess chlorine was driven out by a current of CO_2 until the mixture was decolorized. After dilution of the dioxane solution with ice water, 2 g of the chloro derivative was obtained in the form of colorless plates with m.p. 240—252° (dec. from 200°). *

Found %: Cl 12.01; N 9.55. $C_{12}H_7O_5N_2Cl$. Calculated %: Cl 12.05; N 9.51.

From 2 g of o-carboxydimethoxybenzalbarbituric acid and the chlorine evolved from 1 g of potassium permanganate and 5.5 ml of concentrated hydrochloric acid there was obtained 2.07 g of the chloro derivative in the form of colorless plates with m.p. 185—186° (dec. from 130°).

Found %: Cl 10.10; N 7.95. $C_{14}H_{11}O_7N_2Cl$. Calculated %: Cl 10.10; N 7.90.

c) <u>Action of potassium iodide on the bromo derivative of o-carboxydimethoxybenzalbarbituric acid</u>. Three g of the sodium salt of the bromo derivative of o-carboxydimethoxybenzalbarbituric acid and 1.5 g of potassium iodide, dissolved in 8 ml of water, were heated in a water bath at 50—60° for 5 hours. After decolorization of the reaction mixture with saturated sodium bisulfite solution and acidification with hydrochloric acid,there was isolated about 1.5 g of o-carboxydimethoxybenzalbarbituric acid, which gave no melting-point depression with the acid obtained earlier.

On reaction of the sodium salt of the bromo derivative of o-carboxybenzalbarbituric acid with potassium iodide, o-carboxybenzalbarbituric acid was obtained.

Two g of bromo-o-carboxydimethoxybenzalbarbituric acid, mixed with 10 ml of water and 0.85 g of potassium iodide, gave 1.15 g of a substance which, after recrystallization from large amounts of water (needles), did not melt at 300° or more. * *

Found %: C 52.65; H 3.55; N 8.80. $C_{24}H_{14}O_{10}N_4$. Calculated %: C 52.66; H 3.45; N 8.78.

On reduction by zinc in an acetic acid medium the substance was converted to a mixture of o-carboxydimethoxybenzal- and benzylbarbituric acids.

When 1 g of the bromo derivative of o-carboxydimethoxybenzalbarbituric acid was heated for 6 hours with 0.5 g of zinc in·anhydrous alcohol (or dioxane), a substance was obtained, which, when mixed with the substance obtained in the preceding experiment, did not melt on heating to 300° or more.

SUMMARY

1. It has been shown that chlorine and bromine under mild conditions can replace hydrogen at the ethylenic bond of o-carboxybenzalbarbituric acids, but does not add to the bond.

---

*The substance melted throughout a wide range even after many purifications by reprecipitation from dioxane solution with ice water.
* *On heating above 300° the substance dried up and charred.

2. It has been found that on treatment of the bromo derivatives of benzalbarbituric acids with potassium iodide,debromination takes place, the free benzalbarbituric acid being formed in an alkaline medium and a dimer of this acid being formed in an acid medium.

LITERATURE CITED

[1] E. L Chukhina, J. Gen. Chem. 28, 2582 (1958).*

[2] Synth. Org. Prep. 1, 85 (1949) · [in Russian].

[3] S. Racine, Ann. Chim. 239, 89 (1887).

_____
* Original Russian pagination. See C. B. Translation.

CONDENSATION OF ACETALS, KETALS, AND ORTHOESTERS WITH VINYL ETHERS

SYNTHESIS OF β - ALKOXY - ALDEHYDES AND α, β -UNSATURATED ALDEHYDES

I. N. Nazarov, S. M. Makin, and B. K. Kruptsov

Moscow Institute of Fine Chemical Technology

The possibility of the condensation of acetals with vinyl ethers was first mentioned in 1939 [1].

However, the mechanism of this reaction was established later by Hoaglin and Hirsch, who studied the condensation of a number of acetals of saturated aldehydes with various vinyl ethers in the presence of boron trifluoride as catalyst [2].

$$CH_3CH\genfrac{}{}{0pt}{}{OR}{OR} + CH_2{=}CH{-}OR \rightarrow CH_3CHCH_2CH\genfrac{}{}{0pt}{}{OR}{OR}$$

with OR substituent on the CH of the product.
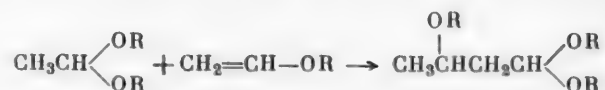
The reaction takes place as a result of splitting-off of an acetal alkoxy group and addition of the fragments formed to the double bond of the vinyl ether. In this case an alkoxy acetal is formed, which can react according to the same scheme with another vinyl ether molecule, and as a result of the reaction, a mixture of alkoxy acetals is obtained.

To decrease the formation of secondary condensation products, it is expedient to use a 2- to 3-fold excess of acetals in the reaction. In the addition of the acetals of α, β -unsaturated aldehydes to vinyl ethers, equimolar quantities of the reagents are taken, since the rate of addition of an α, β -unsaturated acetal is much greater than the rate of addition of the α, β -saturated alkoxy acetals formed in the reaction, as was shown by B. M. Mikhailov [3] and O. Isler [4].

We studies the addition of the diethyl acetals of acetaldehyde, propionaldehyde, butyraldehyde, and isobutyraldehyde to vinyl ethyl and propenyl ethyl ethers. $FeCl_3$ and $(C_2H_5)_2O \cdot BF_3$ were used as catalysts. The use of $FeCl_3$ gave slightly better yields. In all cases a 2- to 3-fold excess of the aldehyde acetal was used in the reaction. Besides products of the addition of one molecule of vinyl ethyl ether to the acetal, products of the addition of two vinyl ethyl ether molecules were isolated. Benzaldehyde and furfural diethyl acetals formed condensation products in good yields with equimolar quantities of vinyl ethyl ether.

In the preceding papers [5, 6] we showed that acetone ketals in the presence of $(C_2H_5)_2O \cdot BF_3$ can easily add to vinyl ethers to form 1,1,3-trialkoxy-3-methylbutanes. In the present work we investigated the condensation of ketals with vinyl ethyl and propenyl ethyl ethers in greater detail. We studied the effect of different catalysts $[(C_2H_5)_2O \cdot BF_3, FeCl_3, TiCl_4, AlCl_3, ZnCl_2, SnCl_4, SnCl_2]$ on the yield of condensation product. The best catalyst proved to be $FeCl_3$. When $(C_2H_5)_2O \cdot BF_3$ was used, the yield of product in some cases was about half as great as when $FeCl_3$ was used. Use of the other enumerated catalysts gave practically no condensation products.

We carried out condensations of the ketals of acetone, ethyl methyl ketone, cyclohexanone, cyclopentanone, and 2,2-dimethyltetrahydropyrone-4 with vinyl ethyl and propenyl ethyl ethers. The yield of condensation product depends to a great degree both on the structure of the ketal used in the reaction and on that of the vinyl alkyl ether. Reaction conditions, constants and yields of the substances obtained are given in Table 1. The ketals and acetals were prepared by a method reported by us [7], using tetraalkoxysilanes.
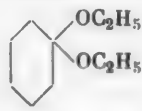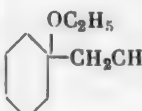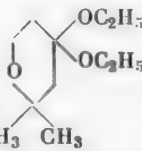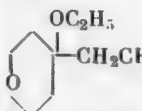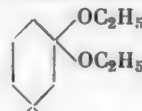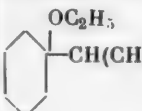
TABLE 1

Condensation Products of Acetals, Ketals, and Orthoformic Ester with Vinyl Ethers

No.	Acetal, ketal, or orthoester (A)	Vinyl ether (B)	Ratio (B : A)	Condensation product*
1	$CH_3CH(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 2.5	$CH_3CHCH_2CH(OC_2H_5)_2$ (I), with OC_2H_5
2	$CH_3CH_2CH(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 2.5	$CH_3CH_2CHCH_2CH(OC_2H_5)_2$ (II), with OC_2H_5
3	$CH_3CH_2CH_2CH(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 3	$CH_3CH_2CH_2CHCH_2CH(OC_2H_5)_2$ (III), with OC_2H_5
4	$(CH_3)_2CHCH(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 2.5	$(CH_3)_2CHCHCH_2CH(OC_2H_5)_2$ (IV), with OC_2H_5
5	$CH_3CH(OC_2H_5)_2$	CH_3, $CH=CHOC_2H_5$	1 : 2	$CH_3CHCH(CH_3)CH(OC_2H_5)_2$ (V), with OC_2H_5
6	$CH_3CH_2CH(OC_2H_5)_2$	CH_3, $CH=CHOC_2H_5$	1 : 2	$CH_3CH_2CHCH(CH_3)CH(OC_2H_5)_2$ (VI), with OC_2H_5
7	$CH_3CH(OC_2H_5)_2$	C_2H_5, $CH=CHOC_2H_5$	1 : 3	$CH_3CHCH(C_2H_5)CH(OC_2H_5)_2$ (VII), with OC_2H_5
8	Ph–$CH(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 1	Ph–$CHCH_2CH(OC_2H_5)_2$ (VIII), with OC_2H_5
9	furyl–$CH(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 1	furyl–$CHCH_2CH(OC_2H_5)_2$ (IX), with OC_2H_5
10	$(CH_3)_2C(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 1.3	$(CH_3)_2CCH_2CH(OC_2H_5)_2$ (X), with OC_2H_5
11	$(CH_3)(C_2H_5)C(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 2.5	$(CH_3)(C_2H_5)CCH_2CH(OC_2H_5)_2$ (XI), with OC_2H_5
12	$(CH_3)_2C(OC_4H_9)_2$	$CH_2=CHOC_4H_9$	1 : 2	$(CH_3)_2CCH_2CH(OC_4H_9)_2$ (XII), with OC_4H_9
13	cyclopentyl $(OC_2H_5)_2$	$CH_2=CHOC_2H_5$	1 : 2	cyclopentyl–$CH_2CH(OC_2H_5)_2$ (XIII), with OC_2H_5

---

*The reaction was carried out with $FeCl_3$ as catalyst in all cases.

* *The reaction was carried out in the presence of $(C_2H_5)_2O \cdot BF_3$.

* * *When $SnCl_4$ was used, the yield of product was 32%.

Yield, reckoned on the vinyl ether (in %)	boiling point (pressure in mm)	d_{20}^{20}	n_D^{20}	MR_D found	MR_D calc.	Found % C	Found % H	Calculated % C	Calculated % H
	Constants					Found %		Calculated %	
70.0	73—76° (13)	0.8795	1.4130	53.86	53.31	63.16, 62.85	11.49, 11.53	63.12	11.65
71.0	83—85 (10)	0.8821	1.4125	57.53	57.92	64.42, 64.50	11.81, 11.85	64.66	11.84
63.6	99—103 (13)	0.8730	1.4139	—	—	—	—	—	—
60.0	95—96 (12)	0.8787	1.4136	62.15	62.34	66.23, 65.96	12.10, 11.70	66.00	12.00
59.0	80 (10) 71—73 (7)	0.8800	1.4117	58.14	57.92	67.76, 64.64	11.52, 11.58	64.66	11.84
60.0	89—91 (10)	0.8833	1.4160	62.15	62.34	66.06, 65.90	11.93, 12.17	66.00	12.00
51.7	104—106 (20)	0.8832	1.4171	62.29	62.34	66.11, 66.01	12.14, 12.17	66.01	12.00
81.0	140 (10)	0.9643	1.4705	—	—	—	—	—	—
72.3	122—124 (10)	0.9880	1.4458	65.48	65.67	64.20, 64.25	9.19, 9.06	64.43	9.15
63.8**	77 (9)	0.8813	1.4145	58.01	57.92	64.55, 64.45	11.80, 11.77	64.66	11.84
69.6	98—100 (13)	0.8927	1.4198	61.95	62.33	65.85, 65.80	11.71, 11.71	66.00	12.00
52.0**	145—147 (8)	0.8726	1.4298	85.55	85.63	71.04, 71.16	12.38, 12.36	70.76	12.58
33.8***	111—113 (7)	0.9355	1.4388	64.85	64.96	68.02, 68.04	11.06, 11.23	67.78	11.34

TABLE 1 (continued)

No.	Acetal, ketal, or orthoester (A)	Vinyl ether (B)	Ratio (B):(A)	Condensation product
14	cyclohexane–OC$_2$H$_5$, OC$_2$H$_5$	CH$_2$=CHOC$_2$H$_5$	1 : 2	cyclohexane–OC$_2$H$_5$, –CH$_2$CH(OC$_2$H$_5$)$_2$ (XIV)
15	tetrahydropyran ring (O)–OC$_2$H$_5$, OC$_2$H$_5$	CH$_2$=CHOC$_2$H$_5$	1 : 2	tetrahydropyran ring (O)–OC$_2$H$_5$, –CH$_2$CH(OC$_2$H$_5$)$_2$ (XV)
16	(CH$_3$)$_2$C(OC$_2$H$_5$)$_2$	CH$_3$–CH=CHOC$_2$H$_5$	1 : 3	(CH$_3$)$_2$CCH(CH$_3$)CH(OC$_2$H$_5$)$_2$ with OC$_2$H$_5$ (XVI)
17	cyclohexane–OC$_2$H$_5$, OC$_2$H$_5$ (CH$_3$ CH$_3$)	CH$_3$–CH=CHOC$_2$H$_5$	1 : 3	cyclohexane–OC$_2$H$_5$, –CH(CH$_3$)CH(OC$_2$H$_5$)$_2$ (XVII)
18	CH(OC$_2$H$_5$)$_3$	CH$_2$=CHOC$_2$H$_5$	1 : 3	CH$_2$[CH(OC$_2$H$_5$)$_2$]$_2$ (XVIII)
19	CH(OC$_2$H$_5$)$_3$	CH$_3$–CH=CHOC$_2$H$_5$	1 : 3	CH$_3$CH[CH(OC$_2$H$_5$)$_2$]$_2$ (XIX)
20	CH(OC$_2$H$_5$)$_3$	C$_2$H$_5$–CH=CHOC$_2$H$_5$	1 : 3	CH$_3$CH$_2$CH[CH(OC$_2$H$_5$)$_2$]$_2$ (XX)
21	CH(OC$_2$H$_5$)$_3$	(CH$_3$)$_2$C=CHOC$_2$H$_5$	1 : 3	(CH$_3$)$_2$C[CH(OC$_2$H$_5$)$_2$]$_2$ (XXI)

Acetone dibutylketal was prepared by the transetherification method from acetone diethyl ketal, by heating with butanol and simultaneously distilling off the ethanol formed.

Orthoesters, like acetals and ketals, condense easily with vinyl ethers in the presence of acid catalysts. There are a number of patent claims on the possibility of addition of orthoformic ester to vinyl ethyl ether [8]. This condensation was thoroughly studied by T. V. Protopopova and A. P. Skoldinov [9]; therefore it was of interest to study this reaction with vinyl ethers having substituents in the vinyl group. It was found that orthoformic ester also reacts easily with propenyl ethyl, butenyl ethyl, and isobutenyl ethyl ethers in the presence of FeCl$_3$ as catalyst. In this case the corresponding diacetals of substituted malonic dialdehydes are obtained.

$$CH(OC_2H_5)_3 + \underset{R'}{\overset{R}{C}}=CHOC_2H_5 \longrightarrow (C_2H_5O)_2CH\underset{R'}{\overset{R}{C}}CH(OC_2H_5)_2$$
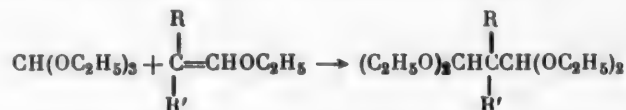
The yield of condensation product decreases as the number and size of substituents in the vinyl group increases (Table 1). This method is very convenient for the preparation of the extremely interesting and as yet little-studied derivatives of malonic dialdehyde.

It was of interest to use the derivatives of 1,1,3-triethoxybutane obtained by us, for conversion to β-alkoxy aldehydes and α, β-unsaturated aldehydes. We found that β-alkoxy aldehydes are easily prepared by briefly heating the derivatives of 1,1,3-triethoxybutane with dilute phosphoric acid. By this method a number of β-alkoxy aldehydes, listed in Table 2, were obtained in good yields.

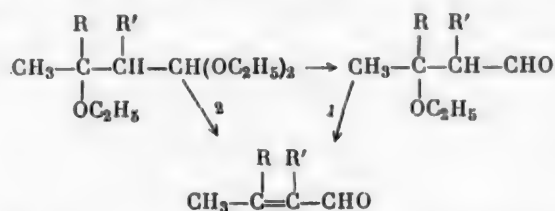Substituted 1,1,3-trialkoxybutanes were converted to α, β-unsaturated aldehydes by two methods:

1) Liquid-phase pyrolysis of β-alkoxy aldehydes in the presence of acid catalysts (we used acid salts of phosphoric acid, and also p-toluenesulfonic acid). This method of synthesizing unsaturated aldehydes is new and

Yield, reckoned on the vinyl ether (in %)	Constants			MR_D		Found %		Calculated %	
	boiling point (pressure in mm)	d_{20}^{20}	n_D^{20}	found	calc.	C	H	C	H
60.7*	128 (10)	0.9402	1.4443	69.23	69.58	68.57, 68.98	11.51, 11.56	68.87	11.59
38.0	160—162 (20)	0.9648	1.4448	75.78	75.84	63.25, 63.40	10.16, 10.11	63.64	10.27
45.8	88—89 (10)	0.8908	1.4188	61.98	62.33	65.76, 65.72	11.81, 11.89	66.00	12.00
21.7	134—136 (10)	0.9483	1.4520	73.82	74.19	69.59, 69.44	11.62, 11.52	69.72	11.70
81.8	92—93 (8)	0.9185	1.4091	59.32	59.57	59.61, 59.65	10.91, 10.89	59.97	10.98
70.0	98.5—100 (8)	0.9164	1.4138	64.00	64.19	61.56, 61.20	11.21, 11.08	61.50	11.18
66.4	101—103 (8)	0.9133	1.4165	68.44	68.58	63.06, 63.08	11.36, 11.20	62.88	11.36
35.5	103.5—104.5 (11)	0.9132	1.4172	68.37	68.58	62.88, 62.73	11.32, 11.18	62.88	11.36

*With $(C_2H_5)_2O \cdot BF_3$ as catalyst, the yield of product was 32%; with $SnCl_2$ it was 10%.

apparently general. The aldehydes obtained by this method are listed in Table 3.

2) Heating of derivatives of 1,1,3-triethoxybutane with dilute acids. α, β-Unsaturated aldehydes obtained by this method may contain small amounts of β-alkoxy aldehydes as impurities. In this case it is expedient to distil the product obtained, with a small amount of mono-basic ammonium phosphate.

$$CH_3-\underset{\underset{OC_2H_5}{|}}{\overset{\overset{R}{|}}{C}}-\overset{\overset{R'}{|}}{CH}-CH(OC_2H_5)_2 \xrightarrow{} CH_3-\underset{\underset{OC_2H_5}{|}}{\overset{\overset{R}{|}}{C}}-\overset{\overset{R'}{|}}{CH}-CHO$$

$$CH_3-\overset{\overset{R}{|}}{C}=\overset{\overset{R'}{|}}{C}-CHO$$

Crotonic, β-methylcrotonic, γ-methylcrotonic, tiglic, and cyclohexylideneacetic aldehydes were prepared by the method described above.

EXPERIMENTAL

Acetone dibutyl ketal. A mixture of 230 g of acetone diethyl ketal and 550 g of butanol was heated in a flask provided with a herringbone column 30 cm high. The flask was kept at a temperature such that ethanol was

TABLE 2

No.	β-Alkoxy aldehyde		Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Yield (in %)
1	OC$_2$H$_5$ $\mid$ CH$_3$CHCH$_2$CHO	(XXII)	47.5—49°(20)	1.4056	0.8927	69.5
2	OC$_2$H$_5$ $\mid$ CH$_3$CH$_2$CHCH$_2$CHO	(XXIII)	150—155	1.4211	0.9084	70.0
3	OC$_2$H$_5$ $\mid$ (CH$_3$)$_2$CCH$_2$CHO	(XXIV)	49.5—50 (13)	1.4192	0.8904	75.2
4	OC$_2$H$_5$ $\mid$ CH$_3$CHCH(CH$_3$)CHO	(XXV)	140—145	1.4171	0.8941	78.3
5	OC$_2$H$_5$ $\mid$ (CH$_3$)$_2$CHCHCH$_2$CHO	(XXVI)	61—63 (12)	1.4186	0.8851	67.2
6	OC$_2$H$_5$ $\mid$ cyclopentyl—CH$_2$CHO	(XXVII)	90—92 (12)	1.4526	0.9688	80.0
7	OC$_2$H$_5$ $\mid$ cyclohexyl—CH$_2$CHO	(XXVIII)	103—105 (13)	1.4559	0.9667	82.3

slowly distilled off at 78—80°. After about 200 ml of ethanol was driven off, the residue was distilled in vacuo. There was obtained 150 g (46%) of acetone dibutyl ketal, b.p. 68—70° (7 mm), n_D^{20} 1.4105.

1,1,3-Triethoxy-2-methylbutane (V). Into a three-necked flask provided with mechanical stirrer, dropping funnel, thermometer, and reflux water condenser were put 515 g of acetaldehyde diethyl acetal and 0.8 g of FeCl$_3$. The flask being cooled with ice water (0—4°), 150 g of propenyl ethyl ether was added from the dropping funnel during 2.5 hours. The mixture was stirred for 2 more hours at room temperature and then neutralized with sodium methoxide, washed from the precipitate with water, and extracted with ether. The ethereal extract was dried with potash and distilled. There was obtained 205.5 g of 1,1,3-triethoxy-2-methylbutane.

Along with 1,1,3-triethoxy-2-methylbutane, 20 g of the secondary condensation product 1,1,3,5-tetraethoxy-2,4-dimethylhexane was isolated.

B.p. 135—138° (15 mm), n_D^{20} 1.4292, d_4^{20} 0.9107, MR$_D$ 82.28; Calc. 82.66.

A 350 g quantity of the original acetaldehyde diethyl acetal was recovered from the reaction.

1-Ethoxy-1-(2,2-diethoxyethyl) cyclohexane (XIV). To a mixture of 86 g of cyclohexanone diethyl ketal and 0.1 g of FeCl$_3$ at 0°, with stirring, 18 g of vinyl ethyl ether was added from a dropping funnel during 1 hour. The mixture was stirred for 2 more hours at room temperature and treated as in the preceding experiment. After distillation, 37 g of 1-ethoxy-1-(2,2-diethoxyethyl) cyclohexane was obtained (Table 1). Yield 60.7%, reckoned on the vinyl ethyl ether or 74%, reckoned on the reacted ketal.

A 50.7 g quantity of cyclohexanone diethyl ketal was recoverd from the reaction.

The other trialkoxy compounds listed in Table 1 were similarly prepared.

1,1,3,3-Tetraethoxy-2-methylpropane (XIX) A mixture of 48 g of orthoformic ester and 0.1 g of FeCl$_3$ was heated to 30°, and 10.8 g of propenyl ethyl ether was added from a dropping funnel during 1 hour, with stirring. The stirring was continued for 1.5 hours more at 45°. The mixture was neutralized with sodium carbonate and

TABLE 3

No.	α,β-Unsaturated aldehyde obtained by pyrolysis of the β-alkoxy aldehyde	Conditions of preparation			Boiling point (pressure in mm)	n_D^{20}	Melting point of 2,4-dinitrophenylhydrazone	Yield (in %)
		temp. of pyrolysis	catalyst	reaction time (in hours)				
1	CH₃CH=CHCHO (XXIX)	150°	NH₄H₂PO₄	5	101–102°	1.4372	189–190°	68.0
2	CH₃CH₂CH=CHCHO (XXX)	190	NH₄H₂PO₄	1	127–129	1.4470	158.5–159	70.0
3	(CH₃)₂C=CHCHO (XXXI)	160–170	NH₄H₂PO₄	0.75	65(64)	1.4564	179.5–180	72.0
4	CH₃CH=C(CH₃)CHO (XXXII)	150–180	p-CH₃C₆H₄SO₃H	0.5	115–116	1.4450	215–216	67.5
5	[cyclohexylidene]=CHCHO (XXXIII)	200	NH₄H₂PO₄	0.5	77–80(12)	1.4855	193–194	70.25

distilled in vacuo. There was obtained 20.5 g (70%) of 1,1,3,3-tetraethoxy-2-methylpropane.

Thirty g of orthoformic ester was recovered from the reaction.

The other tetraalkoxy compounds listed in Table 1 were similarly prepared.

β-Ethoxyisovaleraldehyde (XXIV). A mixture of 25 g of 1,1,3-triethoxy-3-methylbutane, 30 ml of 5% H₃PO₄, and a few crystals of hydroquinone was vigorously stirred at 85° for 1.5 hours and then neutralized with sodium bicarbonate and extracted with ether. The ether extract was dried with magnesium sulfate and distilled. After 2 fractional distillations, 12.0 g of β-ethoxyisovaleraldehyde was obtained. MR_D 36.94; calc. 36.18.

Found %: C 64.60, 64.39; H 10.57, 10.53. C₇H₁₄O₂. Calculated %: C 64.58; H 10.84.

Semicarbazone, m.p. 148.5–149°.

Found %: N 22.14, 22.72. C₈H₁₇O₂N₃. Calculated %: N 22.43.

The other β-ethoxy aldehydes listed in Table 2 were similarly prepared.

β-Methylcrotonaldehyde (XXXI). a) A mixture of 13 g of β-ethoxyisovaleraldehyde and 0.5 g of NH₄H₂PO₄ was heated in a Favorskii flask at 160–170°. The ethanol and β-methylcrotonaldehyde formed in the reaction were distilled off during 45 minutes at 78–130°. The resulting distillate (12.5 ml) was redistilled in vacuo. Six g of β-methylcrotonaldehyde was obtained (see Table 3).

Crotonic γ-methylcrotonic, tiglic and cyclohexylideneacetic aldehydes were synthesized by a similar method. Their 2,4-dinitrophenylhydrazones corresponded to literature data [10–13] (see Table 3).

b) A mixture of 25 g of 1,1,3-triethoxy-3-methylbutane and 30 ml of 10% hydrochloric acid was heated at 50° for 1 hour, with vigorous stirring. The mixture was then neutralized with solid sodium bicarbonate, extracted with ether, and dried with magnesium sulfate. After fractional distillation 8.1 g (78.0%) of β-methylcrotonaldehyde was obtained.

Crotonaldehyde (XXIX) and γ-methylcrotonaldehyde (XXX) were similarly prepared in yields of 51 and 61%, respectively (see Table 3).

SUMMARY

1. The condensation of a number of acetals and ketals, and also orthoformic ester, with vinyl ethyl ether and various β-substituted vinyl ethers has been investigated.

2. The conversion of derivatives of 1,1,3-trialkoxybutanes to β-alkoxy aldehydes and α, β-unsaturated aldehydes has been studied.

3. A new method of synthesis of α, β-unsaturated aldehydes by pyrolysis of β-alkoxy aldehydes is proposed.

LITERATURE CITED

[1] M. Muller-Cuhradi and K. Pierch, C. A. 33, 8210 (1939); U. S. Pat. 2165962 (1936).

[2] R. J. Hoaglin and D. H. Hirch, J. Am. Chem. Soc. 71, 3468 (1949).

[3] B. M. Mikhailov and L. S. Povarov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1957, 1239.*

[4] O. Isler, H. Lindlar and M. Montavon et al., Helv. Chim. Acta 39, 249 (1956).

[5] I. N. Nazarov, S. M. Makin, and B. K. Kruptsov, Proc. Acad. Sci. USSR 117, 823 (1957).

[6] I. N. Nazarov, S. M. Makin, B. K. Kruptsov, and V. A. Mironov, J. Gen. Chem. 29, 111 (1959).*

[7] I. N. Nazarov, S. M. Makin, B. K. Kruptsov, and V. A. Mironov, J. Gen. Chem. 29, 106 (1959).*

[8] M. E. Hultquist, C. A. 43, 4291 (1949); U. S. Pat. 2459076 (1949); J. W. Copenhaver, C. A. 45, 1166 (1951); U. S. Pat. 2527533 (1950; F. Nagasawa and E. Kobayshi, C. A. 48, 5211 (1954); Jap. Pat. 4321 (1952).

[9] T. V. Protopopova and A. P. Skoldinov, J. Gen. Chem. 27, 57 (1957).*

[10] H. Hibbert, J. Am. Chem. Soc. 37, 1759 (1915).

[11] E. E. Royals and K. C. Brannock, J. Am. Chem. Soc. 76, 1180 (1954).

[12] R. Heilman and R. Glenat, C. r. 240, 877 (1955).

[13] M. Julia and J. Surzur, C. r. 238, 2426 (1954).

---

* Original Russian pagination. See C. B. Translation.

LIQUID-PHASE AND VAPOR-PHASE METHODS OF OBTAINING VINYL AND DIENIC ETHERS

SYNTHESIS OF α, β-UNSATURATED ALDEHYDES AND THEIR ACETALS

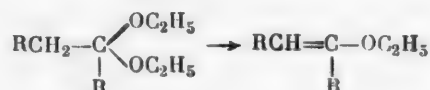I. N. Nazarov, S. M. Makin, and B. K. Kruptsov

The M. V. Lomonosov Moscow Institute of Fine Chemical Technology

The vapor-phase pyrolysis of acetals and alkoxy acetals, leading to vinyl and dienic ethers, was studied by us recently [1, 2]. The 1-alkoxybutadienes and 1-alkoxyisoprenes obtained in this manner have already found utility in the synthesis of polyene compounds [3].

In this paper we studied the synthesis of various substituted alkoxydienes, which up to now have remained completely unstudied. In addition to the vapor-phase method, it also seemed of interest to investigate the liquid-phase method of obtaining vinyl, and especially, dienic ethers.

The liquid-phase pyrolysis of acetals, ketals, and alkoxy acetals was accomplished by heating them in the presence of acid catalysts (acid salts of phosphoric acid and p-toluenesulfonic acid), with simultaneous removal of the alcohol and unsaturated ethers formed in the reaction by distillation.

When the diethyl acetals of acetaldehyde and propionaldehyde, and the diethyl ketal of acetone, are heated in a rectification column, or in a Favorskii flask with a long fractionating column (60-100 cm), in the presence of a small amount of p-toluenesulfonic acid, the distillate is a mixture of the corresponding vinyl ether and alcohol.

$$RCH_2-C \underset{OC_2H_5}{\overset{OC_2H_5}{\big<}} \quad \longrightarrow \quad RCH = C - OC_2H_5$$
$$\underset{R}{\big|} \qquad\qquad\qquad \underset{R}{\big|}$$

The alcohol is removed by washing with water. The yield of the vinyl ethers ranges from 40-45%. This comparatively low yield is due to the fact that during the distillation of the alcohol and vinyl ether a part of the original acetal or ketal is also carried out as a vapor. The pyrolysis reaction goes to greater completion and much more rapidly when the higher boiling acetals and ketals are employed.

The heating of the diethyl ketals of cyclopentanone and cyclohexanone in the presence of $NH_4H_2PO_4$ leads to the formation of the corresponding unsaturated ethers in 80-82% yield. The vinyl ethers that we synthesized by the liquid-phase method are summarized in Table 1.

The acetals and ketals needed for the indicated reactions were obtained by the method that we had developed earlier employing tetraalkoxysilanes [4].

A detailed study of the condensation of various acetals and ketals with vinyl ethers had been made by us in previous papers [2, 5]. The 1,1,3-trialkoxybutane derivatives obtained from this condensation we now used to obtain the substituted alkoxydienes via catalytic decomposition, employing both the liquid-phase and the vapor-phase methods.

In the case of liquid-phase pyrolysis, the substituted 1,1,3-trialkoxybutanes were heated in a Favorskii flask fitted with a long fractionating column, in the presence of an acid catalyst ($NH_4H_2PO_4$).

TABLE 1
Liquid-Phase Pyrolysis of Acetals and Ketals

Expt. No.	Acetal or ketal	Catalyst	Temperature in still pot	Temperature In vapors	Time of process (in hr)	Vinyl ether	n_D^{20}	Boiling point (pressure in mm)	Yield (in %)
1	CH₃CH(OC₂H₅)₂	p-CH₃C₆H₄SO₃H	110—120°	78°	6	CH₂=CHOC₂H₅ (I)	1.3780	36—38°	40.0
2	CH₃CH₂CH(OC₂H₅)₂		165—170	80	5.5	CH₃CH=CHOC₂H₅ (II)	1.3988	69—71	40.2
3	(CH₃)₂C(OC₂H₅)₂		130	80	4	CH₃—C=—OC₂H₅(III)	1.3918	61—62	45.3
4	OC₂H₅ OC₂H₅	NH₄H₂PO₄	165	131	2	OC₂H₅ (IV)	1.4385	62—64 (60)	83.0
5	OC₂H₅ OC₂H₅		180	155	2.5	OC₂H₅ (V)	1.4560	46(8)	80.1

The alkoxydiene and alcohol were distilled off as fast as they were formed. To obtain a high yield of the alkoxydienes, it is very important to keep the temperature of the distilling mixture not exceeding the boiling point of the obtained dienic ether. When heated in the presence of acid catalysts, the acetals of α, β-unsaturated aldehydes are also capable of being converted into alkoxydienes, which was shown by us on the example of the acetals of crotonaldehyde and β-methylcrotonaldehyde.

The alkoxydienes synthesized by us, the conditions of their synthesis, and their constants, are all given in Table 2.

The above-described alkoxydienes can also be obtained easily by the vapor-phase method, as was described by us in a previous communication [2].

The passage of the proper 1,1,3-trialkoxybutane derivatives over acid salts of phosphoric acid at 300-315° gave 1-ethoxy-1,3-pentadiene (VIII), 1-ethoxy-2-methyl-1,3-butadiene (XI), 1-butoxy-3-methyl-1,3-butadiene (XII), and 1-β-ethoxyvinyl-Δ^1-cyclohexene (XV). The conditions used to synthesize these compounds are given in Table 3.

The vapor-phase method can also be used to synthesize 2-alkoxydienes. The passage of the vapors of 1,3,3-trimethoxybutane and 1,3,3-triethoxybutane over acid salts of phosphoric acid gave 2-methoxy-1,3-butadiene (XVII) and 2-ethoxy-1,3-butadiene (XVIII) in good yield (Table 3).

A study of the liquid-phase pyrolysis of compounds of this type had been made earlier by several authors [6-8].

It seemed of great interest to study the hydrolysis of the 1-alkoxydienes synthesized by us in order to obtain the corresponding unsaturated aldehydes from them. It proved that the 1-alkoxydienes are hydrolyzed with ease in the presence of dilute acids to yield α, β-unsaturated aldehydes.

Using this technique, crotonaldehyde, β-methylcrotonaldehyde and γ-methylcrotonaldehyde were obtained in good yields.

$$\begin{array}{cc} R & R' \\ | & | \\ CH=C-CH=CH-OR \end{array} \rightarrow \begin{array}{cc} R & R' \\ | & | \\ CH_2-C=CH-CHO \end{array}$$
$$R, R' = H, CH_3.$$
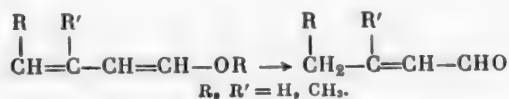
In the presence of acid catalysts, 1-alkoxydienes easily add alcohols in the 1,4 position. This reaction can be used to prepare the acetals of α, β-unsaturated aldehydes in good yield. We obtained

TABLE 2

Synthesis of 1-Alkoxydienes by the Liquid-Phase Method

$$\text{>CH—C—CH—CH<}^{OR}_{OR}\ \longrightarrow\ \text{>C—C—CH—CH—OR}\ \longrightarrow\ \text{>C=C—C=CH—OR}$$

| Expt. No.	Acetal or alkoxyacetal	Temperature in the flask	Temperature in the distillate mixture	Time of process (in hr)	1-Alkoxydiene*	Yield (in %)	boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Analysis found C	Analysis found H	Analysis calculated C	Analysis calculated H
1	CH₃CH=CHCH(OC₂H₅)₂	165°	115°	1.2	CH₂=CH—CH=CHOC₂H₅, (VI)	50.0	65° (150)	1.4615	0.8239	—	—	—	—	—	—
2	(CH₃)₂C=CHCH(OC₂H₅)₂	180	140	0.65	CH₂=C—CH=CHOC₂H₅, (VII) CH₃	63.2	75—78 (100)	1.4623	0.8345	—	—	—	—	—	—
3	CH₃CHClCH₂CH(OC₂H₅)₂ OC₂H₅	190—200	145	3	CH₂=CH—CH=CHOC₂H₅, (VI) CH₃	77.5	—	—	—	—	—	—	—	—	—
4	CH₃CH₂CHCH₂CH(OC₂H₅)₂ OC₂H₅	190—220	130	2.5	CH₃CH=CH—CH=CHOC₂H₅(VIII) C₂H₅	65.0	69—72 (60)	1.4693	0.8324	37.64	35.23	74.68, 74.72	10.93, 10.97	74.95	10.71
5	CH₃CH₂CH₂CHCH₂CH(OC₂H₅)₂ OC₂H₅	190	159	2	CH=CH—CH=CHOC₂H₅, (IX)	68.6	71.5—72.5 (30)	1.4710	0.8272	42.63	39.85	75.81, 75.74	11.11, 10.89	76.13	11.18
6	(CH₃)₂CHCH₂CH₂CH(OC₂H₅)₂ OC₂H₅	200	175	2.5	(CH₃)₂C—C=CH—CH=CHOC₂H₅(X) CH₃	77.8	50 (9)	1.4702	0.8396	41.97	39.85	76.11, 76.44	10.90, 11.20	76.13	11.18
7	CH₃CHClCH(CH₃)CH(OC₂H₅)₂ OC₂H₅	170—200	120	1.5	CH₂=CH—C=CHOC₂H₅, (XI) CH₃	55.0	63—62 (60)	1.4680	0.8312	37.56	35.23	74.80, 75.02	10.83, 10.70	74.95	10.71
8	(CH₃)₂CCH₂CH(OC₂H₅)₂ OC₂H₅	175—190	145	2	CH₂=C—CH=CHOC₂H₅, (VII) CH₃	64.0	—	—	—	—	—	—	—	—	—
9	(CH₃)₂CCH₂CH(OC₄H₉)₂ OC₄H₉	240	116—140	1	CH₂=C—CH=CHOC₄H₉, (XII) CH₃	42.0	92—94 (45)	1.4647	0.8330	46.46	44.47	70.92, 70.81	12.93, 12.85	70.78	12.72
10	(CH₃)₂CCH(CH₃)CH(OC₄H₉)₂- CH₃, CH₃	195	157	2.5	CH₃CH₂—C=CHOC₂H₅, (XIII) CH₃	65.0	59 (22)	1.4726	0.8446	41.99	39.85	76.16, 75.90	11.13, 10.94	76.13	11.18
11	CH₃CH₂CHClCH(CH₃)CH(OC₄H₉)₂ OC₂H₅	205	170	4	CH₃CH=C—CHOC₂H₅, (XIV) CH₃	59.0	70.5—71 (26)	1.4712	0.8417	41.99	39.85	76.02, 76.10	10.96, 11.21	76.13	11.18
12	⬡—CH₂CH(OC₂H₅)₂ OC₂H₅	240	210	2.5	⬡=CH—CHOC₂H₅, (XV)	82.0	94—95 (9)	1.5050	0.9282	48.68	46.89	78.74, 78.68	10.39, 10.72	78.89	10.59
13	⬠—CH₂CH(OC₂H₅)₂ OC₂H₅	220	185	2.5	⬠=CH—CHOC₂H₅, (XVI)	83.2	78 (9)	1.5000	0.9180	44.34	42.27	78.38, 77.95	9.84, 9.94	78.21	10.21

* In all cases the catalyst used was NH₄H₂PO₄.

TABLE 3

Synthesis of Alkoxydienes by the Vapor-Phase Method

Expt. No.	Alkoxy acetal	Catalyst*	Temp. of process	Passage rate (g/hr)	Alkoxydiene		Yield (in %)
1	CH₃C(OCH₃)₂CH₂CH₂OCH₃	MgHPO₄ · Na₂SiO₃	350°	55	CH₂=C—CH=CH₂ (with OCH₃)	(XVII)	69.7
2	CH₃C(OC₂H₅)₂CH₂CH₂OC₂H₅		350	50	CH₂=C—CH=CH₂ (with OC₂H₅, CH₃)	(XVIII)	80.0
3	CH₃CH₂CHCH₂CH(OC₂H₅)₂ (with OC₂H₅)	NaH₂PO₄	300	25	CH=CH—CH=CHOC₂H₅ (with CH₃)	(VIII)	71.5
4	CH₃CHCH(CH₃)CH(OC₂H₅)₂ (with OC₄H₉)		300	25	CH₂=CH—C=CHOC₂H₅ (with CH₃)	(IX)	62.0
5	(CH₃)₂CCH₂CH(OC₄H₉)₂ (with OC₂H₅)		310	30	CH₂=C—CH=CHOC₄H₉ (with CH₃)	(XII)	51.5
6	⬡—CH₂CH(OC₂H₅)₂		315	20	⬡—CH=CHOC₂H₅	(XV)	75.4

*The preparation of the catalysts was described earlier [2].

the diethyl acetal of β-methylcrotanaldehyde from 1-ethoxy-3-methylbutadiene and ethyl alcohol in the presence of traces of hydrochloric acid.

$$CH_2=\underset{\underset{CH_3}{|}}{C}-CH=CH-OC_2H_5 \quad\xrightarrow[\text{HCl}]{C_2H_5OH}\quad \underset{CH_3}{\overset{CH_3}{>}}C=CH-CH\overset{OC_2H_5}{\underset{OC_2H_5}{<}}$$
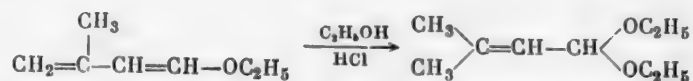
EXPERIMENTAL

Ethyl propenyl ether (II). A mixture of 200 g of propionaldehye diethyl acetal and 3 g of p-toluenesulfonic acid was heated in a Favorskii flask fitted with a 60 cm fractionating column, at 165-170°. In 5.5 hours there distilled 222 ml of distillate with b.p. 65-80°. One gram of fresh p-toluenesulfonic acid was added every 2 hr. The distillate was washed with water, dried over potassium carbonate, and distilled. We obtained 51.3 g of ethyl propenyl ether (II) (see Table 1) and 30 g of starting propionaldehyde diethyl acetal with b.p. 120-125°. The tarry residue weighed 20.8 g.

Vinyl ethyl ether (I) and ethyl isopropenyl ether (III) were obtain in a similar manner.

Ethyl Δ^1-cyclopentenyl ether (IV) and ethyl Δ^1-cyclohexenyl ether (V) (Table 1) were obtained in a similar manner, but here the catalyst used was $NH_4H_2PO_4$ (1.5 g of $NH_4H_2PO_4$ per 50 g of cyclopentanone or cyclohexanone diethyl ketal).

1-Ethoxy-2-methyl-1,3-butadiene (XI) (Table 2). A mixture of 50 g of 1,1,3-triethoxy-2-methylbutane and 1 g of $NH_4H_2PO_4$ was heated in a Favorskii flask at 170-200°. In 1.5 hr the amount of distillate, b.p. 78-120°, was 43 g. The distillate was washed with water, dried over potassium carbonate, and distilled. The yield of product was 15.1 g.

The other 1-alkoxydienes, summarized in Table 2, were obtained in a similar manner.

2-Ethoxy-1,3-butadiene (XVIII)(Table 3). 1,3,3-Triethoxybutane (50 g) was passed in 1 hr, at 350° and a vacuum of 20 mm, through a porecelain contact tube, 60 cm in length and 20 mm in diameter, filled with 60 g of $MgHPO_4 \cdot Na_2SiO_3$. The reaction product was collected in a trap, cooled with a mixture of dry ice and acetone. At reaction end, the product was washed with water, dried over anhydrous potassium carbonate, and distilled. We obtained 20 g (80%) of 2-ethoxy -1,3-butadiene with b.p. 92-96°, n^{20}_D 1.4404.

2-Methoxy-1,3-butadiene (XVII), b.p. 75-77°, n^{20}_D 1.4434, was obtained in a similar manner.

β-Methylcrotonaldehyde. A mixture of 26 g of the ethoxyisoprene (VII) and 14 ml of 2% sulfuric acid was stirred vigorously. The temperature in the flask rose of its own accord from 18° to 38°, and then dropped to 26°. The mixture was stirred for another 1.5 hr at 50°, and then it was neutralized with 15 ml of saturated sodium bicarbonate solution. The aldehyde was extracted with ether, dried over magnesium sulfate, and distilled. We obtained 13.5 g (69.2%) of β -methylcrotonaldehyde with b.p. 133-136°, n^{20}_D 1.4600.

2,4-Dinitrophenylhydrazone, m.p. 179-179.5° [9].

Found %: N 21.23, 21.10. $C_{11}H_{12}O_4N_4$. Calculated %: N 21.21.

Crotonaldehyde, b.p. 101-103°, n^{20}_D 1.4375, was obtained in a similar manner. Yield 45%.

γ-Methylcrotonaldehyde was obtained by heating 1-ethoxy-1,3-pentadiene with 15% H_3PO_4 for 2.5 hr at 80°; b.p. 50-53° (45 mm), n^{20}_D 1.4432. Yield 38%.

2,4-Dinitrophenylhydrazone, m.p. 158-159° [10].

γ-Methylcrotonaldehyde diethyl acetal. Into a three-necked flask fitted with mechanical stirrer, reflux condenser, and thermometer, was charged 11.2 g of 1-ethoxy-3-methyl-1,3-butadiene and 4.6 g of ethyl alcohol. The mixture was cooled to 3° using ice water, and then 1 drop of concd. hydrochloric acid was added. Within a minute the temperature of the mixture rose rapidly to 50°, and then it dropped to room temperature. The mixture was stirred for another 0.5 hr at room temperature, and then it was distilled. We obtained 9.1 g of β-methylcrotonaldehyde diethyl acetal with b.p. 161-163°, n^{20}_D 1.4200 [11].

SUMMARY

1. The synthesis of various substituted 1-alkoxydienes was worked out, using both liquid-phase and vapor-phase techniques. The liquid-phase method was used to obtain a number of substituted vinyl ethers.

2. The hydrolysis of 1-alkoxydienes with dilute acids gave α, β-unsaturated aldehydes.

3. It was established that alcohols, in the presence of acid catalysts, add to 1-alkoxydienes in the 1,4 position to yield the acetals of α, β-unsaturated aldehydes.

LITERATURE CITED

[1] I. N. Nazarov, S. M. Makin and B. K. Kruptsov, Proc. Acad. Sci. USSR 117, 823, (1957). *

[2] I. N. Nazarov, S. M. Makin, B. K. Kruptsov, and V. A. Mironov, J. Gen. Chem. 29, 111 (1959). *

[3] I. N. Nazarov and Zh. A. Krasnaya, Proc. Acad. Sci. USSR 118, 716 (1958). *

[4] I. N. Nazarov, S. M. Makin, B. K. Kruptsov, and V. A. Mironov, J. Gen. Chem. 29, 106 (1959). *

[5] I. N. Nazarov, S. M. Makin, and B. K. Kruptsov, J. Gen. Chem. 29, 3683 (1959). *

[6] H. B. Dykstra, J. Am. Chem. Soc. 57, 2255 (1935).

[7] R. O. Norris, J. J. Verbanc, and J. F. Hennion, J. Am. Chem. Soc. 60, 1159 (1938).

[8] L. A. Favorskaya and N. P. Kopylov-Shakhmatov, J. Gen. Chem. 27, 2406 (1957). *

[9] E. A. Braude and E. R.H. Jones, J. Chem. Soc. 498 (1945).

[10] E. E. Royals, and K. C. Brannock, J. Am. Chem. Soc. 76, 1180 (1954).

[11] F. G. Fischer and K. Löwenberg, Ann. 494, 272 (1932).

IMIDAZOLE DERIVATIVES

XXII. SYNTHESIS AND PROPERTIES OF 5-HYDROXY-1,3-DIMETHYLBENZIMIDAZOLONE

A. V. El'tsov and L. S. Éfros

Lensovet   Leningrad Technological Institute

In earlier communications the observation was made by us that a difference exists in the reactivity of benzimidazolone and benzimidazolone derivatives [1,2]. Thus, a comparison of 5-aminobenzimidazolone (I) with 5-aminobenzimidazole (II) [3] revealed that only the former enters into the azo-coupling reaction; the 1,3-dimethyl derivative of 5-aminobenzimidazolone (III) behaves in exactly the same manner.
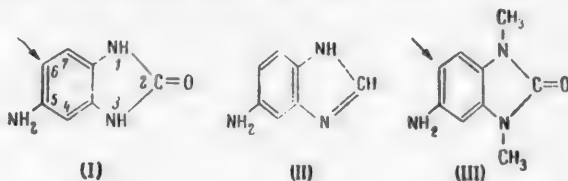
Having identified the azo dyes as being 5-amino-6-arylazo compounds by the conversion of the ortho-diamines obtained from them to phenantriazines, the spectra of which were compared with authentic compounds, we were then able to show [4] that introducing a methyl group on the 6 carbon atom in the molecule (5-amino-6-methylbenzidazolone) renders the amine incapable of coupling with diazonium salts. At the same time, 4,7-dimethyl-5-aminobenzimidazolone readily forms azo dyes when reacted with diazo compounds.

We attempted to explain the high activity shown by a hydrogen atom attached to the carbon atom in the 6 position as due to upsetting the equivalence of the bonds in the benzene ring of the molecule, leading to an increase in the unsaturation between the 5 and 6 carbon atoms in the benzene ring [5].

In connection with the above it seemed of interest to study the behavior of 5-hydroxybenzimidazolone in electrophilic substitution reactions, since, as could be postulated, this compound should readily form azo dyes when reacted with diazo compounds. However, for our investigations we chose the 1,3-dimethyl analog of 5-hydroxybenzimidazolone, since judging from the existing experimental data [1-4, 6], the N-alkylation of a heterocycle increases the solubility and decreases the melting point of benzimidazolone compounds, which facilitates both purification and identification of the studied compounds. As regards reactivity in the benzimidazolone series when compared with that of the corresponding N,N'-dimethyl derivative, then, as our investigations revealed [4], it is always analogous.

We synthesized the previously unknown 5-hydroxy-1,3-dimethylbenzimidazolone (IV) in approximately 80% yield by reacting either 5-methoxy- (V) or 5-ethoxy-1,3-dimethylbenzimidazolone (VI) with concd. hydrobromic acid. It proved that the hydroxy compound corresponding to (VI) shows easy and quantitative coupling with diazotized aniline, in which connection the crude dye (VII) is obtained quite pure (m.p. 199—200°, instead of the 204.5° for the pure compound), and the presence of impurities in it cannot be detected spectrally. The acetylation of dye (VII) with acetic anhydride gave the acetyl derivative (VIII), to which, in harmony with the literature data [7-9], we assigned the structure of the o-acetylazo compound (see the figure, for the spectrum of this compound in methanol solution).

The reduction of dye (VII) with stannous chloride in acid medium gave the aminophenol (IX), which was identified both as the sulfate and as the oxazolone derivative (X), the latter being easily formed when the aminophenol is fused with urea. Oxidation of the aminophenol (IX) with chromic acid gave quinone (XI), which was also synthesized in good yield by the oxidation of phenol (IV) with potassium nitrosodisulfonate (Fremy's salt [10]). The last transformation apparently goes by the mechanism of cationoid substitution through the stages [11, 12]:
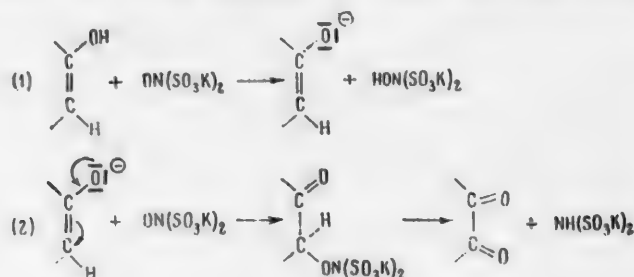
The structure of quinone (XI) was shown by its synthesis from 5,6-dihydroxy-1,3-dimethylbenzimidazolone (XII), obtained from the 5,6-dimethoxy derivative (XIII), which is easily formed by the alkylation of 5,6-dimethoxybenzimidazolone (XIV) with dimethyl sulfate (see scheme). The last compound was reported earlier in the literature [6]; however, the indicated reference apparently contains a typographical error, for the melting point given was 268°, instead of the 246° found by us. Based on both the method of synthesis and the properties, our compound was identical with the compound described by the American authors.
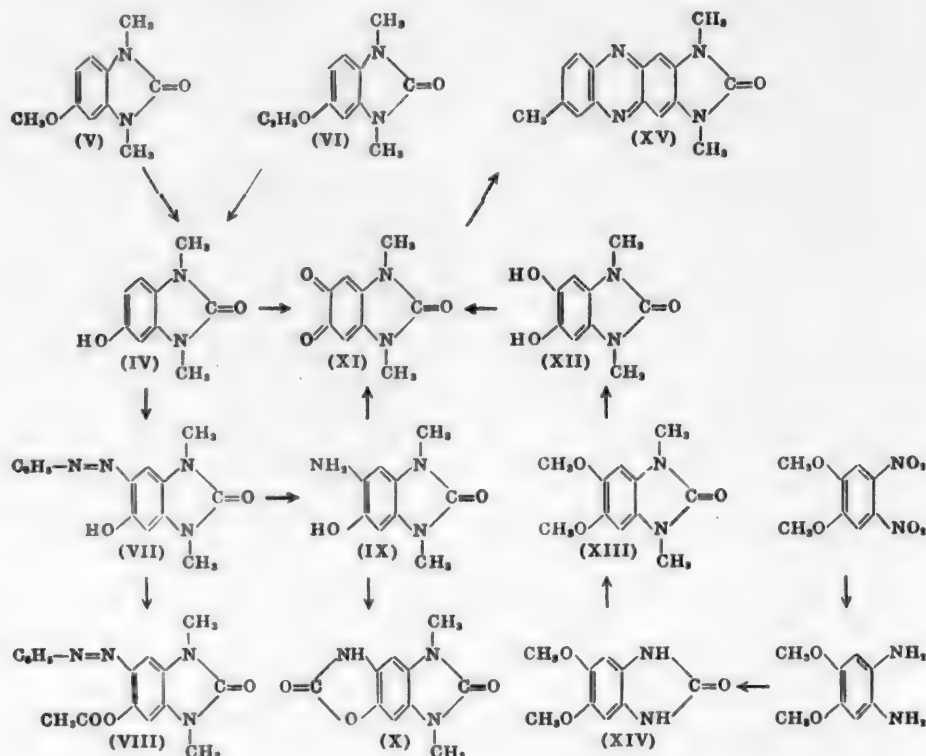
Consequently, on the basis of the accomplished transformations it can be considered as established that both the azo-coupling of 5-hydroxy-1,3-dimethylbenzimidazolone and its oxidation with Fremy's salt take place at the 6 carbon atom, without the formation of any other isomers in noticeable amount.

Quinone (XI) is quite stable, and it fails to change either on long storage in the air or when heated in alcohols, chloroform or acetic acid. It readily condenses with ortho-diamines to yield well-crystallizing azines, one of

which (XV) was purified and characterized by us.

If an attempt is made to compare the chemical properties of the β-hydroxy- and β-amino derivatives of naphthalene with those of the 5-hydroxy and 5-amino derivatives of benzimidazolone studied by us, the attention is involuntarily drawn to the similarity of their behavior in both azo-coupling and oxidation reactions. Both types of compounds show reactivity at only one carbon atom, at the α position in the case of naphtahlene derivatives, and at the 6 position in the case of benzimidazolone derivatives; if this atom is blocked by a methyl group, then reaction does not take place at another free ortho position.

However, the conclusion, based on such an analogy, that increased unsaturation exists between the 5 and 6 carbon atoms in the benzimidazolone nucleus cannot be considered as resting on an adequate foundation [13], even though it is supported by certain other considerations [4].

As is known, 5-hydroxyhydrindene (XVI) is both easily coupled [14] and oxidized with Fremy's salt to yield predominantly 6-substituted derivatives, and yet even a partial "fixation" of the double bond between the 5 and 6 carbon atoms in the hydrindene molecule fails to exist [16]. It should be added that attaching methyl groups to either the 4 or the 6 carbon atom in 5-hydroxyhydrindene does not prevent the compound from coupling at a free ortho position [17, 18].

The reaction of electrophilic substitution at one of the ends of the aromatic bond can testify to the higher order of this bond only in the case where the activity of the reaction center is determined by the presence of such a bond [13]. This is true in the case of a naphthalene, but whether it is also valid for a benzimidazolone can be reliably shown only by measuring the length of the carbon—carbon bonds in the molecule.

Absorption spectra of solutions in methanol.

1) Dye (VII) ($\underline{c}$ 2.73 · 10^{-5} M.; λmax 276, 351, and 419; λmin 255, 304, and 380 mμ);
2) acetyl derivative (VIII) ($\underline{c}$ 3.18 · 10^{-5} M.; λmax 270, 371 mμ; λmin 253 and 297 mμ). An SF-4 spectrophotometer was used to take the spectra at 2 mμ intervals, except in the extreme zones, where they were taken at 1 mμ intervals; the layer thickness was 10.0mm.

Consequently, the experimental results obtained in the present study cannot be considered as decisive proof of the validity of the earlier expressed theory that increased unsaturation exists between the 5 and 6 carbon atoms in a benzimidazolone (although this theory is not being discarded), but they can serve as a stimulus for conducting further experimental investigations in the domain of the chemistry of benzimidazolone and its derivatives.

(XVI)

EXPERIMENTAL *

5-Hydroxy-1,3-dimethylbenzimidazolone (IV). A mixture of 25 g of 5-methoxy-1,3-dimethylbenzimidazolone [6] and 150 ml of concd. hydrobromic acid was heated in sealed tubes for 5 hr at 150°. The highly colored reaction solution was evaporated to dryness, and the residue was recrystallized from a very small volume of alcohol. 5-Hydroxy-1,3-dimethylbenzimidazolone was obtained as colorless crystals with m.p. 212°; the compound is soluble in petroleum ether and benzene, difficulty soluble in chloroform and water, and soluble in alcohol, acetone, and dioxane. Yield 79.5%.
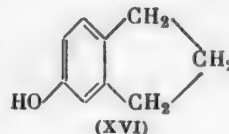
———————————
*Melting points are uncorrected.

The same compound was also obtained in 82% yield by a similar treatment of 5-ethoxy-1,3-dimethyl-benzimidazolone [6].

Found %: C 60.55; H 5.68; N 16.04, 15.95. $C_9H_{10}O_2N_2$. Calculated %: C 60.66; H 5.65; N 15.72.

5,6-Dioxo-1,3-dimethylbenzimidazolone (XI). a) Oxidation of 5-hydroxy-1,3-dimethylbenzimidazolone (IV). * A solution of 1 g of 5-hydroxy-1,3-dimethylbenzimidazolone in 30 ml of methanol was added at 10° to a solution of 2.8 g of Fremy's salt [19] in 150 ml of water and 40 ml of 0.167N KH_2PO_4 solution. The operation was repeated 10 times, and the combined highly colored solutions were kept at 8° for 1 hr. The obtained precipitate was filtered, while the mother liquor was repeatedly extracted with chloroform. The combined extract was dried over fused sodium sulfate, and then evaporated in vacuo to dryness. The residue was added to the filtered crystalline product, and the whole was recrystallized from alcohol. Yield 6 g, based on the pure compound.

b) Oxidation of 5-hydroxy-6-amino-1,3-dimethylbenzimidazolone (IX). To an ice-cooled mixture of 0.2 g of 5-hydroxy-6-amino-1,3-dimethylbenzimidazolone sulfate and 0.8 ml of 20% H_2SO_4 was added a solution of 0.2 g of CrO_3 in 1 ml of water. After standing for 1 hr, the solution was repeatedly extracted with chloroform, the extract dried over fused sodium sulfate, and the residue, after distilling off the solvent, was recrystallized from alcohol. We obtained 0.080 g of the quinone.

c) Oxidation of 5,6-dihydroxy-1,3-dimethylbenzimidazolone (XII). A solution of 0.39 g of 5,6-dihydroxy-1,3-dimethylbenzimidazolone in 15 ml of water was treated with a solution of 1.85 g of potassium ferricyanide in 10 ml of water. The quinone was extracted with chloroform and then recrystallized from alcohol. We obtained 0.3 g of the quinone.

When cooled slowly, 5,6-dioxo-1,3-dimethylbenzimidazolone crystallizes from alcohol as coarse dark-red needles, softening at 236—238°, showing complete liquefaction at 243—244°. The compound is soluble in water, pyridine, acetic acid, chloroform and dioxane, more difficultly soluble in benzene, acetone, and alcohols, and insoluble in petroleum ether. Decolorization, accompanied by a brisk evolution of gas, is observed when an alcohol solution of the quinone is treated with phenylhydrazine. Hydrosulfite in water solution also decolorizes the quinone with the formation of the leuco compound, which slowly changes back to the original compound when kept in the air.

Found %: C 55.95; H 3.96; N 14.54, 14.69. $C_9H_6O_3N_2$. Calculated %: C 56.25; H 4.19; N 14.58.

Azine (XV) from 5,6-dioxo-1,3-dimethylbenzimidazolone and 1,2-diamino-4-methylbenzene. A solution of 0.4 g of the quinone and 0.25 g of the diamine in 10 ml of glacial acetic acid was heated for several minutes. The precipitate obtained on cooling was filtered from the dark-red mother liquor, and then recrystallized from acetic acid. We obtained 0.3 g of light-yellow needles with m.p. 265°. The compound is readily soluble in chloroform, more difficultly soluble in alcohol, acetone, dioxane, and benzene, and insoluble in petroleum ether and water. The solution in concd. sulfuric acid is colored cherry-red.

Found %: N 20.33, 20.22. $C_{16}H_{14}ON_4$. Calculated %: N 20.13.

5-Hydroxy-6-phenylazo-1,3-dimethylbenzimidazolone (VII). A solution of 0.2 g of 5-hydroxy-1,3-dimethyl-benzimidazolone and 0.159 g of sodium carbonate in 4 ml of water, prepared by heating in a small flask, was cooled to 5°, and then treated with a solution of 0.246 g of phenyldiazonium fluoborate in 6 ml of water. The reaction mass was stirred vigorously for 30 min, and then the the deposited azo dye was transferred quantitatively to a Schott filter. The precipitate was washed with 100 ml of distilled water, and then dried at 105° to constant weight. The azo dye, obtained in quantitative yield, melted at 198—200°. One recrystallization from alcohol gave the azo compound as long red needles with a constant m.p. of 204.5°.

The absorption spectra of both the crude and purified products proved to be identical within the limits of accuracy of the spectrophotometer (+2%). The dye is very soluble in chloroform, soluble in dioxane, acetone, benzene, acetic acid, and carbon tetrachloride, and difficultly soluble in alcohol and petroleum ether.

Found %: C 63.53; H 5.27; N 20.05, 19.82. $C_{15}H_{14}O_2N_4$. Calculated %: C 63.83; H 5.00; N 19.85.

---

* Jointly with B. Serebryan.

<u>5-Hydroxy-6-phenylazo-1,3-dimethylbenzimidazolone acetate (VIII)</u>. A mixture of 2 g of the azo compound and 25 ml of acetic anhydride was refluxed for 20 min. The solution after cooling was diluted with an equal volume of water, and the obtained precipitate was recrystallized from alcohol. We obtained 0.9 g of the compound as slender light-yellow needles with m.p. 189—191°. The product is readily soluble in acetic acid, chloroform, benzene, dioxane, and acetone, more difficultly soluble in alcohol, and very difficultly soluble in water and petroleum ether.

Found %: N 17.54, 17.27. $C_{17}H_{16}O_3N_4$. Calculated %: N 17.28.

<u>5-Hydroxy-6-amino-1,3-dimethylbenzimidazolone (IX)</u>. Stannous chloride was added, with heating and stirring, to a suspension of 2.2 g of the azo dye in 20 ml of concd. hydrochloric acid until the reaction mass became colorless. The obtained tin complex of the aminophenol was filtered, then dissolved in water, and the tin was pre-cipitated with hydrogen sulfide. The solution was evaporated in vacuo to dryness, the residue was dissolved in 25 ml of water, and the solution was first decolorized in the cold with charcoal, and then treated with sodium acetate. The obtained slender needles of the free aminophenol were filtered, washed on the filter with water, then with alcohol, and finally with ether. After drying in vacuo, over P_2O_5, the product failed to melt at 300°, and was insoluble in alcohol, ether, benzene, and acetone. We obtained 0.97 g of the compound.

For analysis, the aminophenol was recrystallized from dilute sulfuric acid, and then dried in vacuo over P_2O_5 to constant weight. The slender colorless needles of the aminophenol sulfate darken rapidly in the air.

Found %: C 44.72; H 5.29; S 6.65, 6.53. $C_9H_{11}O_2N_3 \cdot \frac{1}{2} H_2SO_4$. Calculated %: C 44.62; H 4.93; S 6.62.

<u>1,2-(N,N'-Dimethyl)-benzimidazolono-4,5-oxazolonobenzene (X)</u>. A mixture of 1 g of the aminophenol hydrochloride and 1 g of urea was fused in a porcelain crucible at 200°. After cooling, the solid melt was dissolved in warm 3% NaOH solution with the addition of hydrosulfite, after which the solution was decolorized with carbon, and the product was precipitated with hydrochloric acid. The compound was rapidly recrystallized twice from a large volume of water, and then dried at 105°. We obtained 0.2 g of slender colorless needles that failed to melt at 310°, were difficultly soluble in water, alcohol, dioxane, and acetic acid, and insoluble in benzene, petroleum ether, and chloroform.

Found %: C 54.53; H 4.28; N 19.36. $C_{10}H_9O_3N_3$. Calculated %: C 54.79; H 4.14; N 19.17.

<u>5,6-Dimethoxybenzimidazolone (XIV)</u>. A charge of 27 g of 4,5-dinitroveratrole (m.p. 131° [20]), 6 g of freshly prepared Raney nickel [21] and 150 ml of methanol was placed in a 600 ml steel autoclave, and the reaction mass was agitated under a hydrogen pressure of 100 atm for 2 hr at 80°. The catalyst was filtered while the solution was diluted with 1 liter of ether and then saturated with gaseous hydrogen chloride. The highly colored precipitate of 4,5-diaminoveratrole hydrochloride was filtered, washed on the filter with ether (3 × 50 ml), dried in an oven at 80°, and then fused with 30 g of urea in a porcelain crucible for 1 hr at 190—200°. The cold melt was dissolved in 100 ml of 18% NaOH, treated with carbon, and the highly colored solution was cooled to 0°. The sodium salt of 5,6-dimethoxybenzimidazolone, obtained as a crystalline precipitate was filtered, washed on the filter with cold 20% NaOH, and then without drying, was dissolved in 250 ml of hot water. After decolorization with carbon, the hot solution was neutralized with concd. hydrochloric acid, and the precipitate was filtered, and dried at 105°. We obtained 15 g of slightly yellow plates with m.p. 245—246°. After recrystallization from dioxane, the thin, colorless, glistening platelets of 5,6-dimethoxybenzimidazolone melted at 246°. and not at 268°, as indicated in the literature [6]. The compound is soluble in acetic acid and pyridine, difficultly soluble in water and alcohol, and insoluble in acetone, petroleum ether, chloroform, and benzene.

Found %: C 55.40; H 5.17; N 14.59. $C_9H_{10}O_3N_2$. Calculated %: C 55.67; H 5.19; N 14.43.

<u>5,6-Dimethoxy-1,3-dimethylbenzimidazolone (XIII)</u>. To a solution of 5 g of 5,6-dimethoxybenzimidazolone in 50 ml of 8% NaOH, heated to 80—90°, was added dropwise, with vigorous stirring, 5 ml of dimethyl sulfate in 5 min. After stirring for 30 min at the same temperature, the solution was treated with 6 g of NaOH, and then 5 ml of dimethyl sulfate was added in drops. The reaction mass was stirred at the boil for another 30 min, and then evaporated to dryness on the water bath. The residue was extracted with hot benzene for 4 hr, the extract was evaporated to dryness, and the product was recrystallized from a very small volume of toluene. We obtained 5.3 g of heavy, colorless, coarse crystals that melted at 170.5—172°. The substance is readily soluble in water, alcohol, chloroform, benzene, dioxane, acetic acid, carbon tetrachloride, and acetone, and is insoluble in petroleum ether.

Found %: C 59.80, 59.51; H 6.34, 6.18; N 12.69, 12.54. $C_{11}H_{14}O_3N_2$. Calculated %: C 59.45; H 6.35; N 12.61.

5,6-Dihydroxy-1,3-dimethylbenzimidazolone (XII). A mixture of 2 g of 5,6-dimethoxy-1,3-dimethylbenzim-idazolone and 15 ml of concd. hydrobromic acid was heated in a sealed tube for 2 hr at 150°. The precipitate that deposited on cooling was filtered from the highly-colored mother liquor, and then recrystallized repeatedly from aqueous alcohol and from alcohol; the last recrystallizations were made in the presence of small amounts of hydrosulfite. We obtained 0.6 g of slender colorless needles that melted with profound darkening at 266°, and proved to be difficultly soluble in water and in organic solvents. When dissolved in either water or alcohol, the substance oxidizes in the air to the quinone.

Found %: C 55.26; H 5.25; N 14.40, 14.31. $C_9H_{10}O_3N_2$. Calculated %: C 55.66; H 5.19; N 14.42.

SUMMARY

It was established that both the azo-coupling of the new 5-hydroxy-1,3-dimethylbenzimidazolone and its oxidation with Fremy's salt take place at the 6 carbon atom.

LITERATURE CITED

[1] L. S. Éfros and A. V. El'tsov, J. Gen. Chem. 28, 441 (1958).*

[2] L. S. Éfros and A. V. El'tsov, J. Gen. Chem. 28, 2174 (1958).*

[3] L. S. Éfros and B. A. Porai-Koshits, J. Gen. Chem. 23, 959 (1953).*

[4] L. S. Éfros and A. V. El'tsov, J. Gen. Chem. 28, 941 (1958).*

[5] L. S. Éfros and A. V. El'tsov, Trans. Latvian State Univ. 15, 81 (1957).

[6] R. Clark and A. Pessolano, J. Am. Chem. Soc. 80, 1657 (1958).

[7] A. Burawoy and I. Markowitsch, Lieb. Ann. 504, 71 (1933).

[8] P. Ramart-Lucas, M. Grumez, and M. Martynoff, Bull. Soc. Chim. 12, 814 (1946).

[9] P. Ramart-Lucas and C. Dufour, C. r. 230, 1076 (1950).

[10] H. Teuber and N. Götz, Ber. 87, 1236 (1954).

[11] H. Teuber and W. Rau, Ber. 86, 1036 (1953).

[12] H. Teuber, Angew. Chem. 68, 420 (1956).

[13] G. M. Badger, Quarterly. Revs. 5, 147 (1951).

[14] W. Mills and I. Nixon, J. Chem. Soc. 1930, 2510.

[15] H. Teuber and G. Staiger, Ber. 88, 802 (1955).

[16] W. Hückel, Theoretical Principles of Organic Chemistry [Russian translation], 2, (1958) p. 538.

[17] L. Fieser and W. Lothrop, J. Am. Chem. Soc. 58, 2050 (1936).

[18] L. Fieser and W. Lothrop, J. Am. Chem. Soc. 59, 945 (1937).

[19] F. Raschig, Schwefel- und Stickstoffstudien (Leipzig, 1949) p. 149.

[20] H. Verneulen, Rec. trav. chim. 48, 969 (1929).

[21] Organic Syntheses [Russian translation], Coll. Vol. 3, p. 338.

Received March 21, 1958

*Original Russian pagination. See C. B. Translation.

ADDITION OF ORGANOMAGNESIUM COMPOUNDS TO
ETHYLIDENEMALONIC ESTER

V. P. Gol'mov and Ch'ai K'un

Odessa State University

Although it is possible to obtain alkylmalonic esters containing secondary radicals in conventional manner from alkyl halides and sodiomalonic ester, still in most cases the corresponding halo derivatives (especially those containing highly branched radicals) are difficultly available. In addition, secondary reactions (formation of ethers and of unsaturated compounds), noticeably reducing the yield of desired product, are frequently observed when sodiomalonic ester is reacted with secondary alkyl halides.

A second method for obtaining substituted malonic esters of the above indicated structure is the addition of organomagnesium compounds to alkylidenemalonic esters, and, in particular, to ethylidenemalonic ester.

This reaction proceeds in accordance with the following scheme:

$$R-MgX + CH=C-\overset{\overset{\displaystyle OC_2H_5}{|}}{C}=O \rightarrow R-\overset{}{CH}-\overset{}{C}=\overset{\overset{\displaystyle OC_2H_5}{|}}{C}-OMgX \xrightarrow{\text{hydrolysis}}$$

(with CH_3 and $COOC_2H_5$ substituents)

$$\rightarrow R-\overset{\overset{}{|}}{CH}-CH(COOC_2H_5)_2.$$
$$\underset{CH_3}{|}$$
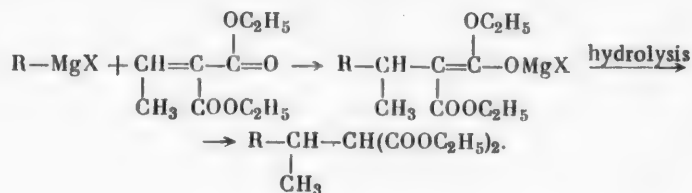
As far as we know, this reaction has been described in the literature for only two examples. The two examples are α-methyl-β-(α-naphthyl)ethylmalonic ester [1], synthesized by the reaction of ethylidenemalonic ester with the Grignard reagent obtained from 1-(chloromethyl)naphthalene, and 1-methyl-5-n-hexenylmalonic ester [2], obtained by reacting ethylidenemalonic ester with 4-pentenylmagnesium bromide.

In order to study the indicated reaction in somewhat greater detail, we conducted some experiments in the present investigation on the addition of the organomagnesium compounds obtained from bromobenzene, o-bromotoluene, propyl bromide,and isopropyl bromide to ethylidenemalonic ester. When the Grignard reagent was phenylmagnesium bromide, we obtained α-phenylethylmalonic ester, previously described in the literature and synthesized from sodiomalonic ester and α-chloroethylbenzene [3], and also by the addition of methylmagnesium iodide to benzylidenemalonic ester [4]. Saponification of the indicated ester gave us α-phenylethylmalonic acid [4], and the latter on decarboxylation gave us β-phenylbutyric acid [3]. This experiment again proves that the organomagnesium compound adds in the 1,4 position. The reaction of ethylidenemalonic ester with propylmagnesium bromide gave α-methylbutylmalonic ester, which when saponified gave α-methylbutylmalonic acid, and this acid on decarboxylation gave the previously known β-methylcaproic acid [5].

The reaction of ethylidenemalonic ester with o-tolylmagnesium bromide and isopropylmagnesium bromide gave α-(o-tolyl)ethylmalonic ester and α,β-dimethylpropylmalonic ester, respectively, and these esters when saponified and decarboxylated gave the corresponding di- and monocarboxylic acids.

In our experiments the substituted malonic esters were obtained in yields ranging from 45 to 60%. Consequently, ethylidenemalonic ester reacts more smoothly with Grignard reagents than does isopropylidenemalonic

TABLE 1

Alkylmalonic Esters R − CH − CH(COOC$_2$H$_5$)$_2$
| CH$_3$

R	Yield (in %)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	calc.	%C found	calc.	%H found	calc.
Phenyl	58.5	134° (2)	1.0598	1.4852	71.42	71.18	67.97	68.14	7.46	7.58
o-Tolyl	60.0	142—143 (2.5)	1.0549	1.4860	75.66	75.80	68.95	69.06	7.81	7.91
n-Propyl	60.0	92—93 (2)	0.9731	1.4259	60.55	60.92	62.76	62.61	9.27	9.57
iso-Propyl	45.5	85—87 (2)	0.9788	1.4282	60.48	60.92	62.32	62.61	9.36	9.57

TABLE 2

Alkylmalonic Acids R − CH − CH(COOH)$_2$
| CH$_3$

R	Melting point	%C found	calculated	%H found	calculated
Phenyl	142—143°	63.27	63.45	5.80	5.77
o-Tolyl	116—117	64.58	64.86	6.40	6.36
n-Propyl . . .	91— 93*	54.89	55.17	8.22	8.04
iso-Propyl . . .	89— 90.5	55.20	55.17	8.34	8.04

* From a mixture of benzene and chloroform.

TABLE 3

Alkylacetic Acids R − CH − CH$_2$ − COOH
| CH$_3$

R	Boiling point (pressure in mm)	d_4^{21}	n_D^{21}	MR_D found	calc.	%C found	calc.	%H found	calc.
Phenyl . .	126—128° (1.5)*	1.0701	1.5155	46.25	46.32	73.49	73.17	7.08	7.32
o-Tolyl . .	166—167.5 (12)**	—	—	—	—	73.89	74.16	7.99	7.99
n-Propyl .	100—102 (7)	0.9163	1.4216	36.02	36.16	64.44	64.62	10.47	10.77
iso-Propyl .	90—91.5 (6)	0.9274	1.4251	35.85	36.16	64.54	64.62	10.82	10.77

* The cooled mixture solidified to crystals with m.p. 36.5 − 38.5° (from petroleum ether).

** M.p. 45 − 47°.

ester [6], and the given reaction is suitable for the synthesis of alkylmalonic esters containing secondary radicals, which are difficultly available when their preparation is attempted by the usual technique*.

EXPERIMENTAL

The starting ethylidenemalonic ester was prepared from malonic ester and paraldehyde [7], and it had the following constants: b.p. $86 - 87°$ (3 mm), d_4^{20} 1.0404, n_D^{20} 1.4395; MR_D 46.96.

<u>Reaction of organomagnesium compounds with ethylidenemalonic ester.</u> To a solution of the organomagnesium compound, prepared from 7 g of magnesium, 0.25 mole of halo compound and 100 ml of absolute ether, was added, with ice-water cooling, in drops, with mechanical stirring, 46.5 g of ethylidenemalonic ester. Here a thick yellow oil was obtained, appearing as the lower layer of the mixture. To complete the reaction, the liquid was heated on the water bath for 30 min, then cooled, and the addition product was decomposed with 90 ml of hydrochloric acid (1 : 2). The ether layer was separated, while the water layer was extracted twice with ether. The combined ether extracts were dried over fused calcium chloride, the ether distilled off, and the residue fractionated in vacuo.

The properties of the thus obtained alkylmalonic esters are given in Table 1.

The obtained alkylmalonic esters were saponified by heating them with 10% alcoholic KOH solution for 3 hr; then the solution was diluted with water, the alcohol removed completely by distillation, and the residue, after acidification with sulfuric acid, was extracted with ether. The ether extracts were dried over fused calcium chloride, followed by removal of the ether by distillation. The residual oil soon crystallized [an exception was α-(o-tolyl)ethylmalonic acid, which crystallized only when kept in a desiccator over sulfuric acid for 1.5 months]. The alkylmalonic acids were purified by recrystallization from benzene. The obtained acids are listed in Table 2.

The alkylmalonic acids were decarboxylated by heating them in an oil bath at $150 - 160°$ until the evolution of carbon dioxide ceased. The properties of the alkylacetic acids obtained in this manner are summarized in Table 3.

SUMMARY

1. The addition of organomagnesium compounds to ethylidenemalonic ester gave the following esters: α-phenylethylmalonic, α-(o-tolyl)ethylmalonic, α-methylbutylmalonic and α,β-dimethylpropylmalonic, in yields ranging from 45 to 60%.

2. The given method is suitable for the synthesis of alkylmalonic esters containing highly branched secondary radicals.

LITERATURE CITED

[1] B. Riegel, S. Siegel, and W. M. Lilienfeld, J. Am. Chem. Soc. <u>68</u>, 984 (1946).

[2] E. van Heyningen, J. Am. Chem. Soc. <u>76</u>, 2241 (1954).

[3] E. Fischer and W. Schmitz, Ber. <u>39</u>, 351, 2208 (1906).

[4] E. P. Kohler, Am. Chem. J. <u>34</u>, 132 (1905).

[5] G. Ciamician and P. Silber, Ber. <u>46</u>, 3077 (1913).

[6] V. P. Gol'mov and Z. P. Malevannaya, J. Gen. Chem. <u>28</u>, 3075 (1958).**

[7] Organic Syntheses [Russian translation], Coll. vol. 4, p. 254 (1953).

[8] G. Ad. Holmber, Acta Chem. Scand. <u>12</u>, 229 (1958).

Received November 4, 1958

---

* When our paper was already in print, we learned that analogous experiments had been run simultaneously with ours [8].

** Original Russian pagination. See C. B. Translation.

HERBICIDES AND REGULATORS OF PLANT GROWTH

XXXIII. SYNTHESIS OF SOME HALOPHENOXYALKYLCARBOXYLIC ACIDS AND THEIR DERIVATIVES

N. N. Mel'nikov and S. S. Kukalenko

In previous communications we had described a large number of different halophenoxyalkylcarboxylic acids and their derivatives, containing various substitutents in the aromatic ring [1 − 6], including alkyl-, aryl-, alkoxy-phenoxy- and halophenoxyacetic and butyric acids, and also the corresponding halophenoxyacetones and halo-phenoxyethanols [7], and the halonaphthoxyalkylcarboxylic acids and their derivatives [8]. Of the halo-substituted aryloxyalkylcarboxylic acids, the corresponding chloro- and bromo- derivatives, some of which find quite wide use in agriculture, have been studied in the greatest detail up to now, whereas quite inadequate study has been given to the fluoro-substituted aryloxyalkylcarboxylic acids [9]. The only fluoro derivatives reported in the literature are the o-, m- and p-fluorophenoxyacetic acids [10], fluorophenoxyisobutyric acid [11], 4-methoxy-3-fluorophenoxyacetic acid [12], 2,4-dichloro-5-fluoro- and 2,4-dichloro-3-fluorophenoxyacetic acids [13], and several other compounds, which have been tested as plant herbicides [14]. Based on the existing literature data, some of the fluorine- containing halophenoxyacetic acids function as quite active stimulants of plant growth [13] and as herbicides [14].

In connection with a study of the relationship existing between the physiological activity of halophenoxy-alkylcarboxylic acids on plants and their structure, it seemed of interest to synthesize some new compounds belonging to the indicated type.

The compounds obtained by us and their properties are given in the table.

It should be mentioned that the herbicidal activity of the compounds synthesized by us does not surpass that of the corresponding chlorophenoxyalkylcarboxylic acids.

EXPERIMENTAL

4-Fluorophenol. Obtained by the saponification of p-fluoroanisole with hydrogen bromide in acetic acid. A mixture of 93 g of p-fluoroanisole, 112 ml of acetic anhydride and 205 ml of 40% hydrobromic acid was heated under reflux for 8 hr. Then the solution was diluted with 1.5 liters of water, and the p-fluorophenol was isolated in conventional manner. Yield 55 g (66%), b.p. 86 − 87° (16 mm). From the literature [15]: b.p. 81 − 85° (14 mm).

Found %: C 64.48, 64.27; H 4.79, 4.72. C_6H_5OF. Calculated %: C 64.28; H 4.48.

γ -(4-Fluorophenoxy)butyric acid was synthesized in the same manner as γ -(2,4-dichlorophenoxy)butyric acid [16]. To the sodium ethylate, obtained from 4.75 g of sodium metal and 135 ml of alcohol, was added 32 g of p-fluorophenol and 54 g of 1-chloro-3-bromopropane, and the mixture was heated for 4 hr under reflux. Then the solution was diluted with 100 ml of water, several drops of 20% NaOH solution was added, to a strongly alkaline reaction, the solution extracted with benzene, the benzene distilled off, and the residue was fractionated in vacuo. The yield of γ -(p-fluorophenoxy)propyl chloride was 20 g (38%).

B.p. 130 − 133° (15 mm), d_4^{20} 1.2519, n_D^{20} 1.5125.

Found %: C 56.56; H 5.31. $C_9H_{10}OClF$. Calculated %: C 57.28; H 5.30.

Properties of Halophenoxyalkylcarboxylic Acids and Their Derivatives

Name	Yield (in %)	Temperature — boiling point (pressure in mm)	Temperature — melting point	d_4^{20}	n_D^{20}	Found % C	Found % H	Calculated % C	Calculated % H
4-Fluorophenoxyacetic acid*	65	—	103—104°	—	—	57.28	4.11	56.50	4.11
4-Fluorophenoxyacetate: ethyl	75	147—148° (22)	—	1.1783	1.4870	60.00, 60.55	5.84, 5.74	60.60	5.55
n-butyl	89	150—151 (12)	—	1.1243	1.4840	63.25, 63.47	7.06, 6.90	63.71	6.63
n-octyl	89	172—173 (9)	—	1.0776	1.4830	67.85, 68.13	8.07, 7.96	68.07	8.15
2-Chloro-4-fluorophenoxyacetic acid	67	—	132—134	—	—	47.47	(3.0)	46.94	2.93
γ-(4-Fluorophenoxy)butyric acid	53	—	134—135	—	—	39.15	2.52	38.55	2.40
	50	—	106—107	—	—	61.32	5.98	61.32	5.55
γ-(2-Bromo-4-fluorophenoxy)butyric acid	54	—	102—104	—	—	43.72	4.13	43.32	3.61

* Literature data [18]: m.p. 102 — 103°.

A mixture of 8.3 g of γ-(p-fluorophenoxy)propyl chloride and 7 g of potassium cyanide in 200 ml of alcohol was heated under reflux for 4 hr. After cooling, the reaction mixture was diluted with 50 ml of water, and the nitrile was extracted with benzene. After removal of the benzene, the crude nitrile was saponified by refluxing with 6 g of KOH in 75 ml of 50% alcohol. After saponification, the solution was acidified and then extracted with benzene. The γ-(4-fluorophenoxy)butyric acid was extracted from the benzene solution with 10% aqueous sodium carbonate solution. Acidification of the alkaline solution gave the acid as a precipitate. The yield was 4.5 g (50%). The properties of the acid and of the other compounds synthesized by us are given in the table.

The esters of 4-fluorophenoxyacetic acid were prepared by esterifying the acid with the proper alcohol in the presence of a drop of sulfuric acid, with azeotropic distillation of the reaction water, as is described in the literature [17].

Halogenation of 4-fluorophenoxyalkylcarboxylic acids. The halogenation of the 4-fluorophenoxyacetic and γ-(4-fluorophenoxy)butyric acids was run in carbon tetrachloride, in which connection the chlorinations were run at $20 - 30°$, and the brominations at the boiling point of the solution. At the end of reaction, the hydrogen halide was removed by blowing with dry air, followed by removal of the carbon tetrachloride by distillation, and then the obtained acid was recrystallized from a suitable solvent. To accelerate the bromination, several milligrams of iodine was added to the reaction mixture. The obtained compounds are listed in the table.

SUMMARY

To study the relationship between structure and the physiological activity on plants, we synthesized a number of previously unknown halophenoxyalkylcarboxylic acids and their esters.

LITERATURE CITED

[1] S. S. Nametkin, N. N. Mel'nikov, and Yu. A. Baskakov, J. Gen. Chem. 19, 1151 (1949).*

[2] S. S. Nametkin, N. N. Mel'nikov, and K. S. Bokarev, Proc. Acad. Sci. USSR 68, 77 (1949).

[3] S. S. Nametkin, N. N. Mel'nikov, and K. S. Bokarev, Proc. Acad. Sci. USSR 77, 419 (1951).

[4] S. S. Nametkin, N. N. Mel'nikov, and Yu. A. Baskakov, J. Gen. Chem. 21, 2146 (1951).*

[5] N. N. Mel'nikov, R. Kh. Turetskaya, and Yu. A. Baskakov, Plant Physiology 2, 267 (1955).

[6] N. N. Mel'nikov, R. Kh. Turetskaya, and K. S. Bokarev, Proc. Acad. Sci. USSR 90, 921 (1953).

[7] K. S. Bokarev and N. N. Mel'nikov, J. Gen. Chem. 24, 2014 (1954).*

[8] S. S. Nametkin, N. N. Mel'nikov, and Yu. A. Baskakov, J. Gen. Chem. 18, 2019 (1948).

[9] N. N. Mel'nikov, Yu. A. Baskakov, and K. S. Bokarev, Chemistry of Herbicides and Stimulants of Plant Growth [in Russian] (Goskhimizdat, Moscow, 1954).

[10] N. Hayes and G. Branch, J. Am. Chem. Soc. 65, 1555 (1943).

[11] A. Jönsson, Acta Chem. Scand. 7, 596 (1954).

[12] K. Kraft and F. Dengel, Ber. 85, 577 (1952).

[13] K. Klaassens and C. Schoot, Rec. trav. chim. 75, 186 (1956).

[14] H. E. Thompson, C. P. Swanson, and A. G. Norman, Botan. Gaz. 107, 476 (1946).

[15] G. Schiemann and co-workers, J. prakt. Chem. 143, 18 (1935).

[16] M. E. Synerholm and P. W. Zimmerman, Contrib. Boyce Thompson Inst. 14, 369 (1947).

[17] K. S. Bokarev and N. N. Mel'nikov, Trans. Sci. Inst. of Fertilizers and Insectofungicides (Goskhimizdat, Moscow, 1958) 158, p. 269.

[18] C. Suter, E. Lawson, and P. Smith, J. Am. Chem. Soc. 61, 161 (1939).

---

*Original Russian pagination. See C. B. Translation.

CHEMICAL EQUALITY OF THE CARBON ATOMS
IN THE TROPYLIUM ION*

M. E. Vol'pin, D. N. Kursanov, M. M. Shemyakin,
V. I. Maimind, and L. A. Neiman

Institute of Heteroorganic Compounds of the Academy of Sciences of the USSR
and the Institute of Biological and Medicinal Chemistry of the Academy of
Medical Sciences of the USSR

It is assumed that in the seven-membered aromatic system — the tropylium ion [2] — all of the carbon — carbon bonds are alike, and that all of the carbon atoms are equivalent and bear the same portion of the positive charge. However, up to now, there has been no direct proof that such an assumption is valid. An attempt to study the structure of the tropylium chloride molecule by the x-ray technique ended in failure due to the complex nature of the crystal structure [3], while the x-ray data relating to the structure of tropylium iodide and the perchlorate did not permit arriving at any conclusion as to the equivalence of the carbon — carbon bonds due to a "turning" of the seven-membered ring in the crystal.** Both the infrared spectra and the Raman spectra of tropylium salts [4] show a small number of lines, which is in harmony with the high symmetry shown by a seven-membered ring, but this fact by itself is not sufficiently rigid proof that all of the carbon — carbon bonds in the molecule are equivalent.

In this paper our objective was to prove experimentally, using the method of labeled atoms, the chemical equality of all seven carbon atoms in the tropylium ion.
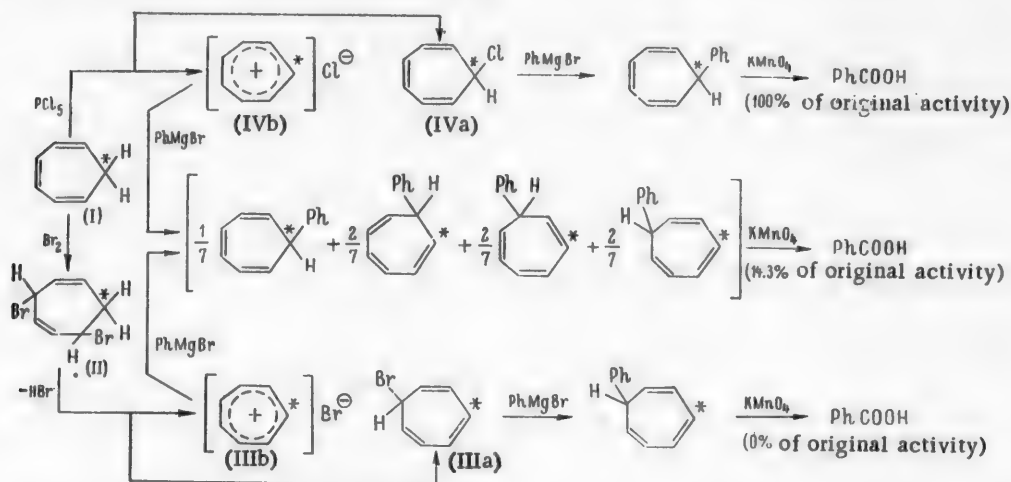
For this purpose the cycloheptatriene (I), labeled with C^{14} in the methlene group,*** was converted by the earlier described procedure [2] to dibromocycloheptatriene-$C^{14}H_2$ (II), the cleavage of HBr from which gave

---

* See [1] for the previous communication.

** Based on the investigations made by A. I. Kitaigorodskii and co-workers.

*** Obtained by the reaction of diazomethane-C^{14} with benzene; here toluene, in which all of the C^{14} is found in the methyl group, is formed at the same time.

TABLE 1

Radioactivity of Tropylium Salts and of Benzoic Acid

Compound	Relative activity			
	direct measurement on paper		measurement as $BaC^{14}O_3$	
	imp/min per mmole	%	imp/min per mmole	%
Tropylium bromide	$5.57 \cdot 10^5$	100	$2.34 \cdot 10^5$	100
Benzoic acid from tropylium bromide	$0.742 \cdot 10^5$	13.3	$0.298 \cdot 10^5$	12.7
Tropylium chloride	$5.55 \cdot 10^5$	100	$2.31 \cdot 10^5$	100
Benzoic acid from tropylium chloride	$0.755 \cdot 10^5$	13.6	$0.294 \cdot 10^5$	12.7

tropylium-C^{14} bromide; the latter by reaction with phenylmagnesium bromide was converted to phenylcycloheptatriene-C^{14}, which on oxidation with potassium permanganate gave benzoic acid.

In dibromocycloheptatriene-$C^{14}H_2$ (II), independent of whether it was formed as the result of 1,2; 1, 4; or 1,6 addition of Br_2 to the double bonds, it is possible for all of the atoms to be linked to C^{14}. Consequently, if a fixed bond between the bromine atom and one of the carbon atoms in the ring (polarized covalent bond or an ionic bond, as in an ionic pair) is retained in the formed tropylium-C^{14} bromide, then this bromine atom proves to be linked to one of the unlabeled carbon atoms, as shown in structure (IIIa). The second possibility here is that all of the carbon atoms in the formed tropylium ion are equivalent and bear the same portion of the positive charge, as shown by structure (IIIb).

The problem as to which of these two structures is valid can be solved in the following manner. If tropylium-C^{14} bromide has structure (IIIa), then replacing the bromine atom by the phenyl radical should lead to a phenylcycloheptatriene in which the phenyl radical is not linked to C^{14}; in such case the benzoic acid formed subsequently by oxidation should prove to be unlabeled (see scheme). If all of the carbon atoms in the tropylium ion are completely equivalent, corresponding to structure (IIIb), then the probability of attack by the phenyl group will be the same for all of them, and for this reason the oxidation product of the phenylcycloheptatriene, namely benzoic acid, should contain $^1/_7$ (i.e., 14.3%) of the original activity. Consequently, depending on the activity of the obtained benzoic acid (0 or 14.3%), it is possible to establish whether tropylium bromide has structure (IIIa) or (IIIb).

To show that the obtained results are independent of the method used to synthesize the tropylium salt, we ran a second series of experiments in which the tropylium-C^{14} salt was obtained by replacing the hydrogen in the CH_2 group of cycloheptatriene-C^{14} by chlorine using phosphorus pentachloride [5]. The thus synthesized tropylium-C^{14} chloride was purified by conversion to the perchlorate, which, when reacted with phenylmagnesium bromide, was converted to the phenylcycloheptatriene, and this compound was then oxidized to benzoic acid. If the tropylium-C^{14} chloride corresponds to structure (IVa), then the benzoic acid that is formed should contain 100% of the original molar activity. If (IVb) is the valid structure, i.e., all of the carbon atoms in the tropylium ion are completely equivalent, then, the same as in the above discussed case, the benzoic acid that is formed should contain $^1/_7$ (14.3%) of the original activity. Consequently, here also the degree of activity shown by the benzoic acid permits deciding between structures (IVa) and (IVb).

We used two different methods to determine the activity of the investigated compounds: by direct measurement on paper (see [6]), and as $BaC^{14}O_3$. The results of the measurements are given in Table 1.

In both series of experiments the found values of the benzoic acid activity (12.7 — 13.6%) lie close to 14.3%, which is the theoretical value to be expected if the carbon atoms in the tropylium ion are all equal (structures IIIb and IVb). The slight reduction in the activity when compared with the theoretical is apparently linked with the isotopic effect [7]. The latter was observed in studying a series of analogous reactions, and was of approximately the same magnitude; thus, when phenyllithium was reacted with chlorocyclohexene [8], the isotopic effect reduced the activity of the benzoic acid (formed when the phencylcyclohexene was oxidized) from 25 to 23%.

TABLE 2

Determination of the Radioactivity of Tropylium Salts and of Benzoic Acid by Direct Measurement on Paper

Compound	Sample wt. (in mg)	Amount of solvent	Expt. no. *	Rate count in (imp/min)	Relative activity (in impulses/min/mmole)
Tropylium perchlorate from tropylium bromide	13.4	1 ml of water	1	382 ± 6	$(5.43 \pm 0.08) \cdot 10^5$
			2	405 ± 7	$(5.76 \pm 0.10) \cdot 10^5$
			3	377 ± 6	$(5.36 \pm 0.08) \cdot 10^5$
			4	382 ± 9	$(5.43 \pm 0.12) \cdot 10^5$
			5	415 ± 9	$(5.89 \pm 0.12) \cdot 10^5$
					Average . . $(5.57 \pm 0.10) \cdot 10^5$
Tropylium perchlorate from tropylium chloride	23.7	1 ml of water	1	699 ± 5	$(5.62 \pm 0.04) \cdot 10^5$
			2	695 ± 15	$(5.58 \pm 0.12) \cdot 10^5$
			3	684 ± 6	$(5.50 \pm 0.05) \cdot 10^5$
			4	684 ± 11	$(5.50 \pm 0.10) \cdot 10^5$
					Average . . $(5.55 \pm 0.08) \cdot 10^5$
Benzoic acid from tropylium bromide	19.4	1 ml of alcohol	1	119 ± 4	$(0.749 \pm 0.025) \cdot 10^5$
			2	117 ± 2	$(0.737 \pm 0.013) \cdot 10^5$
			3	114 ± 3	$(0.718 \pm 0.019) \cdot 10^5$
			4	116 ± 2	$(0.729 \pm 0.013) \cdot 10^5$
			5	122 ± 2	$(0.768 \pm 0.013) \cdot 10^5$
					Average . . $(0.742 \pm 0.017) \cdot 10^5$
Benzoic acid from tropylium chloride	19.4	1 ml of alcohol	1	121 ± 2	$(0.762 \pm 0.013) \cdot 10^5$
			2	121 ± 5	$(0.762 \pm 0.031) \cdot 10^5$
			3	126 ± 2	$(0.792 \pm 0.013) \cdot 10^5$
			4	117 ± 3	$(0.737 \pm 0.019) \cdot 10^5$
			5	114 ± 1	$(0.718 \pm 0.006) \cdot 10^5$
					Average . . $(0.755 \pm 0.016) \cdot 10^5$

* For each experiment we took 10 μ liters of the investigated solution

The obtained results unequivocally show the chemical equality of the carbon atoms in the tropylium ion. The possibility of some of the intermediate reactions (reaction with phenylmagnesium bromide, reaction with PCl_5, conversion of tropylium chloride to the perchlorate) going with a partial transfer of the reaction center does not change the validity of this conclusion. Actually, if tropylium bromide does have structure (IIIa), then if any of the reactions went with a partial transfer of the reaction center, the benzoic acid that is obtained should have an activity intermediate between 0 and 14.3%, while if tropylium chloride has structure (IVa), then the activity of the obtained benzoic acid should lie between 100 and 14.3%. Consequently, the fact that the values found by us for the benzoic acid activity show good agreement in both series of experiments is evidence that the carbon atoms in the tropylium ion are equivalent.

EXPERIMENTAL

1. Preparation of cycloheptatriene-$C^{14}H_2$ and toluene-$C^{14}H_3$ (analogous to [9]). A charge of 2 liters of benzene and 300 ml of 50% KOH solution was placed in a 5-liter porcelain beaker, cooled to $5 - 7°$, and then 150 g of nitrosomethylurea-$C^{14}H_3$* was added in small portions with stirring. The stirring was continued for

* The nitromethylurea-$C^{14}H_3$ was obtained from 440 mg of $C^{14}H_3 NH_2 \cdot$ HCl (total activity 5 γ curies), using the earlier described procedure [10], and then it was made up to 150 g by dilution with unlabeled nitrosomethylurea.

TABLE 3

Determination of the Radioactivity of Tropylium Salts and of Benzoic Acid After Conversion to $BaC^{14}O_3$

Compound	Sample wt. (in mg)*	Rate count (in imp/min)	Relative activity (in imp/min/mmole)
Tropylium chloroplatinate from tropylium bromide	3.61	2805 ± 29	$(2.30 ± 0.023) \cdot 10^5$
	1.91	1558 ± 4	$(2.41 ± 0.006) \cdot 10^5$
	1.89	1505 ± 9	$(2.35 ± 0.014) \cdot 10^5$
	3.39	2629 ± 31	$(2.29 ± 0.025) \cdot 10^5$
			Average . . $(2.34 ± 0.017) \cdot 10^5$
Tropylium chloroplatinate from tropylium chloride	2.18	1606 ± 20	$(2.18 ± 0.027) \cdot 10^5$
	2.30	1806 ± 30	$(2.31 ± 0.038) \cdot 10^5$
	2.51	1985 ± 7	$(2.33 ± 0.008) \cdot 10^5$
	2.91	2413 ± 20	$(2.44 ± 0.020) \cdot 10^5$
			Average . . $(2.31 ± 0.023) \cdot 10^5$
Benzoic acid from tropylium bromide	1.47	360 ± 5	$(0.298 ± 0.004) \cdot 10^5$
	1.96	476 ± 6	$(0.295 ± 0.004) \cdot 10^5$
	2.87	708 ± 8	$(0.301 ± 0.003) \cdot 10^5$
			Average . $(0.298 ± 0.004) \cdot 10^5$
Benzoic acid from tropylium chloride	1.69	400 ± 3	$(0.289 ± 0.002) \cdot 10^5$
	1.82	441 ± 4	$(0.295 ± 0.003) \cdot 10^5$
	1.90	463 ± 5	$(0.297 ± 0.003) \cdot 10^5$
			Average . $(0.294 ± 0.003) \cdot 10^5$

* The amounts of radioactive compounds indicated in the table were diluted with the corresponding unlabeled compounds in such manner that the total amount for the tropylium chloroplatinate was 30.0 mg, while for benzoic acid it was 12.4 mg (these amounts are needed to obtain an "infinitely thick" layer of $BaC^{14}O_3$).

another 15 min, after which the upper layer was decanted, while the water layer was washed several times with benzene. The obtained benzene solution of $C^{14}H_2N_2$, after drying over granulated KOH for an hour, was transferred to a 2.5 liter flask, and then irradiated with ultraviolet light at $5 - 7°$ until the evolution of nitrogen ceased (about 30 hr). The benzene was removed by distillation through a rectification column, and then the residue was distilled. We obtained 3.19 g of a mixture containing about 60% cycloheptatriene-$C^{14}H_2$ and about 40% of toluene-$C^{14}H_3$ (refractometric determination). The mixture had b.p. $112.5 - 114.1°$, and n_D^{20} 1.5121.

2. Preparation of tropylium-C^{14} bromide (analogous to [2]). To a solution of 2.7 g of mixed cycloheptatriene-$C^{14}H_2$ and toluene-$C^{14}H_3$ (containing about 1.6 g of cycloheptatriene-$C^{14}H_2$) in 25 ml of dry CCl_4 was added, with stirring and ice-water cooling, a solution of 2.4 g of bromine in 20 ml of dry CCl_4, in 40 min. After removal of the CCl_4 and toluene-$C^{14}H_3$ by distillation, the residue was heated for 12 hr at 60° and 8 mm, and then for 8 hr at 70° and 0.2 mm. The obtained tropylium-C^{14} bromide was washed with dry CCl_4, recrystallized from anhydrous alcohol (cooling to -50°), and washed with ether. Yield 1.54 g (60%).

3. Preparation of tropylium-C^{14} chloride (analogous to [5]). A solution of 0.5 g of the mixed cycloheptatriene-$C^{14}H_2$ and toluene-$C^{14}H_3$, obtained in Expt. 1, in 20 ml of CCl_4 was treated with 5 g of PCl_5, and the mixture allowed to stand for 24 hr at room temperature. The obtained precipitate was filtered, and the filtrate was used to isolate the toluene-$C^{14}H_3$ (see Expt. 7), while the precipitate was dissolved cautiously in 20 ml of water. Addition of excess 50% $HClO_4$ solution to the obtained tropylium-C^{14} chloride solution gave a precipitate of tropylium-C^{14} perchloroate.

4. Preparation of phenylcycloheptatriene-C^{14}. To a solution of 1.25 g of tropylium-C^{14} bromide in 30 ml of anhydrous ether was added, with stirring, an ether solution of phenylmagnesium bromide (2-fold excess), followed by refluxing the mixture for 20 min. After cooling, the excess phenylmagnesium bromide was decomposed with 20% hydrochloric acid, and the ether layer was separated, washed with 10% hydrochloric acid, water, 10% KOH solution, again with water, and finally it was dried over $CaCl_2$. After removal of the ether, the residue was vacuum-distilled. We obtained 1.16 g of phenylcycloheptatriene-C^{14} (containing a small amount of biphenyl as impurity); yield 94%. Using similar conditions, phenylcycloheptatriene-C^{14} was also obtained from 150 mg of tropylium perchlorate in 10 ml of anhydrous ether.

5. Oxidation of phenylcycloheptatriene-C^{14}. A mixture of 1.16 g of phenylcycloheptatriene-C^{14}, 16 g of $KMnO_4$, 2 ml of 1N NaOH and 200 ml of water was refluxed for 15 hr, after which the MnO_2 precipitate was filtered, the filtrate (after removing the biphenyl* by steam-distillation) evaporated to a volume of $15-20$ ml, the residue acidified with concd. hydrochloric acid, and the benzoic acid was extracted with ether. The ether solution was extracted with 1N NaOH, the alkaline extract acidified with hydrochloric acid, and the obtained $C_6H_5C^{14}OOH$ was recrystallized from water. Yield 130 mg; m.p. $120-122°$.

6. Measurement of the radioactivity (with the help of M. I. Lerman). a) Determination on paper** (see Table 2). Because of their hygroscopy both tropylium bromide and the chloride were first converted to the perchlorate [5]; the benzoic acid was used directly.

On an aluminum target (inside diameter 18 mm) was placed a disk of filter paper (Whatman No. 2) of the same diameter. The weighed sample was dissolved in 1 ml of the solvent (water for tropylium perchlorate, and alcohol in the case of benzoic acid, and 10 μ liters of this solution (amount needed to form a blot over the whole surface of the disk) was placed from an automatic micropipette in the center of the filter disk. After drying in a desiccator over concd. H_2SO_4, the samples were measured using a MST-17 block counter.

b) Determination as barium carbonate (see Table 3). The investigated substance was burned by the "wet method", in which connection both the tropylium bromide and the chloride were first converted to the chloroplatinate [5]. The combustion was run in a modified Barker apparatus [11]. For the oxidation of 30 mg of tropylium chloroplatinate we used a mixture composed of 450 mg of Ag_2CrO_4, 600 mg of Na_2SO_4, 900 mg of $K2CrO_4$, and 7 ml of concd. H_2SO_4 (see [12]). The mixture was heated for 1 hr at $140-150°$, and then it was allowed to stand at room temperature for 1 hr. The evolved $C^{14}O_2$ was absorbed in barium hydroxide solution with constant shaking. The obtained $BaC^{14}O_3$ specimens were prepared by the V. G. Vasil'ev method [13] for measuring in an "infinitely thick" layer. The combustion of the benzoic acid (sample weight 12.4 mg) was run under analogous conditions; the mixture was heated for 45 min at $100°$, and then allowed to stand at room temperature for 1 hr.

7. Isolation of toluene-$C^{14}H_3$ and determination of its isotopic composition. The filtrate obtained in Expt. 3, after removal of the tropylium-C^{14} chloride, was washed with water, concd. hydrochloric acid, water, 40% NaOH solution, again with water, and finally it was dried over $CaCl_2$. After distilling off the CCl_4 in a rectification column, followed by distillation of the residue, the latter was refluxed for 10 hr with 1 g of $KMnO_4$ in 50 ml of water. The benzoic acid was isolated and purified in the same manner as described above. The activity of the benzoic acid, determined after "wet combustion", was $2.46 \cdot 10^5$ impulses/ min/ mmole. In addition, the obtained benzoic acid was decarboxylated by reaction with sodium azide and 100% H_2SO_4 at $50-60°$, using the same conditions as described earlier for the decarboxylation of $CH_3C^{14}OOH$ [14] in the Barker apparatus [11]. The evolved $C^{14}O_2$ was converted to $BaC^{14}O_3$, the activity of which was $2.48 \cdot 10^5$ impulses/ min/ mmole. From this it follows that all of the C^{14} is contained in the methyl group of the obtained toluene.

SUMMARY

The chemical equality of the carbon atoms in the tropylium ion was shown using C^{14}.

---

* By means of special experiments it was shown that biphenyl does not form benzoic acid under these conditions.

** This method of measuring the relative radioactivity is characterized by being extremely simple, since it eliminates the need of burning the substance and forming a precipitate.

LITERATURE CITED

[1] M. E. Vol'pin, D. N. Kursanov, M. N. Shemyakin, V. Maimind, and L. Neyman, Chemistry and Industry 1958, 1261.

[2] W. von E. Doering and L. H. Knox, J. Am. Chem. Soc. 76, 3203 (1954).

[3] E. S. Gould, Acta Cryst. 8, 657 (1955).

[4] W. G. Fately and E. R. Lippincott, J. Am. Chem. Soc. 77, 249 (1955); Koyo Aida, Sci. Repts. Res. Insts. Tohoku Univ. 48, 361 (1956).

[5] D. N. Kursanov and M. E. Vol'pin, Proc. Acad. Sci. USSR 113, 339 (1957).*

[6] D. Jerchel and W. Woticky, Ann. 605, 191 (1957).

[7] S. Z. Roginskii, Theoretical Principles of Isotopic Methods for the Study of Chemical Reactions [in Russian] (Izd. AN SSSR, 1956).

[8] F. Scardiglia and J. D. Roberts, Tetrahedron 1, 343 (1957).

[9] W. E. Doering and L. H. Knox, J. Am. Chem. Soc. 75, 297 (1953).

[10] Organic Syntheses [Russian translation], Coll. Vol. 2, p. 373 (1949).

[11] S. Aronoff, Isotopic Methods in Biochemistry [Russian translation] (IL, 1959), p. 85.

[12] S. Apelgot and S. Mars, Bull. soc. chim. biol. 35, 691 (1953).

[13] V. G. Vasil'ev, J. Anal. Chem. [USSR] 10, 368 (1955).*

[14] E. F. Phares, Arch. Biochem. Biophys. 33, 176 (1951).

*Original Russian pagination. See C. B. Translation.

DEHYDROGENATION OF 2,2-DIMETHYLBUTANE

L. B. Fisher, M. P. Terpugova, V. P. Kuznetsova.
and I. L. Kotlyarevskii

Institute of Chemistry of the Eastern Siberia Branch of the Academy of
Sciences of the USSR

In a previous paper [1] we studied the dehydrogenation of 2,3-dimethylbutane and found that on catalysts from domestic raw materials this reaction goes to considerably greater completion than is true for the dehydrogenation of butane [2]. Thus, under the best conditions, the catalyzate, obtained in 71 − 72% yield, contains 60 − 63% of unsaturated hydrocarbons. Up to 87% of these unsaturates are hexenes, representing approximately equal amounts of 2,3-dimethyl-1-butene and 2,3-dimethyl-2-butene. Besides olefins, the catalyzate contains substantial amounts of dienic hydrocarbons (up to 15%), whereas the dehydrogenation of butane and isopentane, yields only small amounts of dienic hydrocarbons [3 − 7].

TABLE 1

Experiments on the Dehydrogenation of 2,2-Dimethylbutane

Expt. no.	Reaction temperature	Space velocity (liter/liter of catalyst/hr)	Amount (in ml)		Yield of catalyzate (in %)	Characteristics of catalyzate			Yield of unsaturates based on starting product (in %)
			taken	obtained		n_D^{20}	iodine number	unsaturates (in %)	
10	550°	0.5	8.01	5.3	66.16	1.3768	104	34.4	22.76
1		1	6.3	5.3	84.12	1.3762	68	24	20.19
4	570	0.66	4.59	2.6	56.64	1.3852	114	37.7	21.35
5		1	7.92	5.1	64.39	1.3790	105	34.7	22.34
6		2	8.28	6.4	77.29	1.3770	95	31.4	24.27
9		2.5	8.37	6.2	74.07	1.3768	87	29	21.48
3	600	1	6.12	2.5	40.86	1.3900	132	43.6	17.81
7		2	8.19	4.5	54.94	1.3791	118	39	21.43
8		2.5	8.55	4.8	56.14	1.3782	116	38.3	21.50

Remarks: The receiver in which the liquid catalyzate was collected was cooled to −18 to −20°.

Since, as far as we know, studies on the dehydrogenation of disubstituted butanes have not been published, we continued our study of this reaction using 2,2-dimethylbutane. Here it could be postulated that the reaction will go in only one direction with the formation of 2,2-dimethyl-3-butene.

Our study of the dehydrogenation of 2,2-dimethylbutane was made using two different catalysts: a catalyst from domestic raw material, and a commerical catalyst. In the case of the latter, the yield of liquid catalyzate under the optimum conditions was 75 − 77%, and it contained about 32% of unsaturated hydrocarbons. After removal of dissolved gases, the amount of unsaturates in the catalyzate dropped to 25.8%, and this amount was

Amount of catalyst (in ml)	Yield of catalyzate (in %)	Amt. of unsaturated hydrocarbons in the liquid catalyzate (in %)	Degree of conversion of 2,2-dimethylbutane (in %)	Yield of unsaturated hydrocarbons based on 2,2-dimethylbutane (in %)	
				on material passed	on reacted material
10	85.9	33.1	46.9	29.1	70.5
20	87.3	30.6	44.4	26.9	68.9

Remarks: The receiver was cooled to -50 to -55°. The space velocity was equal to 2, and the temperature was 570°.

TABLE 3

Fraction no.	Boiling range	Amount g	Amount (in %)	n_D	Iodine number	Unsaturated hydrocarbons (in %)	Dienic hydrocarbons (in %)	Composition of the fractions, according to the Raman spectra
1	20—30°	15	6.4	1.3548	348	95.5*	—	2-Methyl-1-butene (main product) and methylbutane
2	30—35	5.5	2.4	1.3798	326	107**	13.7	2-Methyl-1,3-butadiene, 2,2-dimethyl-3-butene and 2-methylbutane (traces)
3	35—42	13.0	5.5	1.3788	270	89.3	4.7	2,2-Dimethyl-3-butene (main product)*** and isoprene
4	42—44	8.5	3.6	1.3746	177	58.5	0.3	2,2-Dimethyl-3-butene and 2,2-dimethylbutane
5	44—47.6****	16	6.8	1.3697	38	12.5	—	2,2-Dimethylbutane (main product) and 2,2-dimethyl-3-butene
6	47.6—48.1	46	19.5	1.3688	5	1.6	—	—
7	48.1—48.8	112	47.6	1.3685	0	0	—	—

* The amount of unsaturated hydrocarbons in the 1st fraction was calculated on C_5.

** Both of the double bonds in the dienic hydrocarbons show partial reaction, and therefore the amount of unsaturated hydrocarbons > 100%.

*** After removal of the dienic hydrocarbon, the fraction contained only 2,2-dimethyl-3-butene.

**** The 5th fraction boiled mainly at 47 — 47.6°.

distributed as follows: 33.9% of pentenes and isoprene, 48.4% of 2,2-dimethyl-3-butene (normal reaction product) and 17.7% of isomerization products, mainly tetramethylethylene and 2,3-dimethylbutadiene. These results are quite different from those given in the American patent [8], where it was shown that the dehydrogenation of 2,2-dimethylbutane on an alumina-chromia catalyst gave a 14 — 15% yield of mixed hexenes, analyzing 70% as 2,3-dimethylbutenes.

To determine the role played by the position of the methyl groups in substituted butanes on the course of the thermal dehydrogenation, we studied this reaction on the examples of 2,2- and 2,3-dimethylbutanes and found that here, on quartz, under the optimum conditions for catalytic dehydrogenation, 2,2-dimethylbutane gave half as much unsaturates as 2,3-dimethylbutane.

TABLE 4

Starting hydrocarbons	Yield of catalyzate (in %)	Analysis of catalyzate		Yield of unsaturates based on the crude (in %)
		iodine number	amt. of unsaturates (in %)	
2,2-Dimethyl-butane 2,3-dimethyl-butane	93.3 * 95.6	27 50	8.9 16.6	8.3 15.9

Remarks: Reaction temperature 570°, space velocity 2.
* The Raman spectrum revealed that the catalyzate was
mainly starting 2,2-dimethylbutane with some 2,2-dimethyl-
-3-butene as impurity.

As a result, due to the presence of a quaternary carbon atom in 2,2-dimethylbutane, the dehydrogenation (both catalytic and thermal) of the latter is greatly inhibited when compared with that of 2,3-dimethylbutane, butane, and isopentane.

EXPERIMENTAL

The starting 2,2-dimethylbutane (b.p. $47 - 47.5°$ at 720 mm, n_D^{20} 1.3689) was obtained by the thermal alkylation of isobutane with ethylene under high pressure, which was a special investigation in itself; the structure of the compound was proved by its Raman spectrum.

The dehydrogenations were run in the apparatus described in an earlier paper [1]. The methods used to determine the iodine numbers and the amounts of dienic hydrocarbons are also given in the same reference.

The effect of temperature and of the space velocity was studied using a catalyst from domestic raw material, the preparation of which was worked out by us jointly with M. N. Marushkin and A. P. Belen'kaya [2].

The data on the dehydrogenation of 2,2-dimethylbutane using this catalyst are given in Table 1.

As can be seen from the data in Table 1, the optimum conditions for the reaction are 570° and a space velocity of 2 liters/liter catalyst/hr. The gas evolved under these conditions had the following composition: hydrogen 53.2%, unsaturated hydrocarbons 12%, and saturated hydrocarbons 34.8%.

At 600° and a space velocity of 2 or 2.5, the amount of unsaturates in the catalyzate rose to $38 - 39\%$, but because of increased cracking, the catalyzate yield dropped.

To study the composition, a sufficient amount of the catalyzate was produced on the catalyst under the conditions given in Table 2.

The liquid catalyzate, after removal of the gases (boiling up to 20°), and weighing 235.5 g, was fractionated through a column with an efficiency of 30 theoretical plates, and distilled in the range $20 - 100°$, in which connection 90% of the material distilled in the range $20 - 48.8°$. The catalyzate had an iodine number of 78, and n_D^{20} 1.3741.

The data on the fractional distillation and analysis of the obtained products are summarized in Table 3.

The hydrocarbons in the different fractions were identified by chemical analysis and the Raman spectra. As a result, the 1st and 2nd fractions represent 2-methyl-1-butene and isoprene; the 3rd fraction is mainly 2,2-dimethyl-3-butene with some isoprene as impurity; the 4th and 5th fractions are a mixture of 2,2-dimethyl-3-butene and starting 2,2-dimethylbutane, and the 6th and 7th fractions are unreacted 2,2-dimethylbutane. The still residue (boiling mainly at $59 - 74°$) proved to be a mixture of 2,3-dimethyl-1,3-butadiene (20%) and tetramethylethylene.

Table 4 shows the behavior of 2,2- and 2,3-dimethylbutane when they are subjected to thermal dehydrogenation (on quartz).

SUMMARY

1. The catalytic dehydrogenation of 2,2-dimethylbutane was studied, and it was shown that the principal reaction product is 2,2-dimethyl-3-butene.

2. It was established that the dehydrogenation of 2,2-dimethylbutane is greatly inhibited due to the presence of a quaternary carbon atom in it.

LITERATURE CITED

[1] L. B. Fisher, M. P. Terpugova, and I. L. Kotlyarevskii, Bull. Eastern Affiliation, Acad. Sci. USSR 1957, No. 9, 53.

[2] L. B. Fisher, M. N. Marushkin, and A. P. Belen'kaya, Bull Eastern Affiliation, Acad. Sci. USSR 1957, No. 1, 53.

[3] A. A. Balandin, N. D. Zelinskii, M. N. Marushkin, and L. N. Pavlov, Proc. Acad. Sci. USSR 32, 136 (1941).

[4] N. I. Shuikin, T. P. Dobrynina, E. A. Timofeeva, and Yu. P. Egorov, Bull. Acad. Sci. USSR, Div. Chem. Sci. 1955, 952.

[5] Yu. G. Mamedaliev, M. A. Dalin and T. I. Mamedov, Proc. Azerbaidzhan SSR 11, 13 (1955); 12, 3 (1956).

[6] B. A. Kazanskii, M. N. Marushkin, O. D. Sterligov, and A. P. Belen'kaya, Proc. Acad. Sci. USSR 117, 619 (1957).*

[7] Yu. A. Gorin, A. A. Vasil'ev, and A. N. Makashina, Chem. Industry [USSR] 1, (1958).

[8] U. S. Patent 2,406,688; C. A. 41, 275 (1947).

*Original Russian pagination. See C. B. Translation.

INVESTIGATIONS IN N-SUBSTITUTED INDAZOLE SERIES

II. SYNTHESIS OF ACYLINDAZOLES*

Jao Êrh-Ch'ang and M. N. Shchukina

S. Ordzhonikidze All-Union Chemical-Pharmaceutical Scientific
Research Institute

Since a search for biologically active compounds in the indazole series has received very little attention up to now, we undertook the task of synthesizing a number of derivatives of this heterocycle, containing in their structure some of the groupings characteristic of certain highly active medicinals. For example, acylindazoles, and especially isonicotinoylindazoles, have much in common with the highly active antitubercular compounds derived from isonicotinoyl hydrazide (phthivazide, Salizid, larusan, etc.) [1].

As was shown by the investigations of von Auwers [2], indazole forms two series of acyl derivatives. The unstable 2-substituted derivatives are formed when the reaction is run at low temperature, which rearrange to the stable 1-isomers when heated. The same is also observed for the isonicotinoyl derivatives of indazole. The reaction of indazole with the hydrochloride of isonicotinoyl chloride at $5-10°$ gave us a compound that we assumed to be 2-isonicotinoylindazole, since when heated above its melting point it rearranged to the stable isomer. The latter is also obtained directly if the acylation is run in boiling solvent (benzene — pyridine).

We obtained the isonicotinoylindazoles by heating indazoles with the hydrochloride of isonicotinoyl chloride [5] in pyridine, or a mixture of dry benzene and pyridine, for several hours. For the syntheses we took indazole, 6-nitro-, 6-acetamido-, 6-hydroxy- and 3-chloroindazole. As was to be expected, the diisonicotinoyl derivative was obtained in the case of 6-hydroxyindazole.

It was shown by us that the isonicotinoyl derivatives of indazole and its derivatives are easily hydrolyzed. Here a substituent in the indazole ring affects the stability of the $N-C$ bond between the indazole and the acyl grouping toward hydrolytic agents. The presence of electronegative substituents, like chlorine or the nitro group, reduces the stability. The acylindazoles obtained by us were tested in the Division of Chemotherapy of the All-Union Chemical-Pharmaceutical Scientific Research Institute, and proved to have very little activity. This confirms the conclusion that for antitubercular activity it is insufficient to have only a certain arrangement of the atoms and bonds, but, in addition, it is necessary to retain certain groups. In particular, for antitubercular activity in the series of isonicotinoyl hydrazide derivatives it is necessary to have the hydrazine amino group present, or else the possibility of its easy formation. These factors are absent in the isonicotinoyl derivatives of indazoles. In these compounds, the same as is true of the 1-alkylisonicotinoylhydrazines, and of 1-isonicotinoylpyrazole and its dimethyl derivatives [6], all being inactive toward the tubercle bacillus, the nitrogen linked to the isonicotinoyl radical is devoid of a hydrogen atom. This makes it impossible for isonicotinoylindazoles to form complexes, a property that is inherent in isonicotinoylhydrazine and its hydrazones, and to which a number of authors attribute the antitubercular activity shown by these compounds [7].

EXPERIMENTAL

1-Isonicotinoylindazole. A mixture of 4.92 g of isonicotinic acid and 50 ml of thionyl chloride was heated under reflux for 5 hr. When reaction was done, the excess thionyl chloride was vacuum distilled at the end with the addition of dry benzene. To the suspension of the obtained isonicotinoyl chloride hydrochloride in 30 ml of dry benzene was gradually added, with stirring, a suspension of 3.54 g of indazole in a mixture of

---

40 ml of dry benzene and 6.5 ml of dry pyridine. The mixture was refluxed for 6 hr, after which the benzene solution was evaporated to dryness, and the residue was washed, first with water, and then with sodium bicarbonate solution. We obtained 5.9 g (88.2%) of colorless compound with m.p. 138 — 139°. Two recrystallizations of the 1-isonicotinoylindazole from alcohol raised the m.p. to 140 — 140.5°. Colorless needles, readily soluble in chloroform, ethyl acetate and mineral acids, more difficulty soluble in alcohol, benzene,and ether, and insoluble in petroleum ether.

Found %: C 69.88; H 4.07; N 19.00. $C_{13}H_9ON_3$. Calculated %: C 69.94; H 4.06; N 18.83.

1-Isonicotinoylindazole (0.1 g) was added to 15 ml of 5% hydrochloric acid. Here the free base dissolved, and after some time the hydrochloride separated as colorless crystals. Treatment of this compound with sodium carbonate solution in the cold gave the starting acyl derivative of the indazole, which had m.p. 140°, and failed to depress the melting point when mixed with the pure specimen.

2-Isonicotinoylindazole. To a suspension of 2 g of isonicotinoyl chloride hydrochloride in 20 ml of dry benzene was added, with stirring, at 5 — 10°, a solution of 1.18 g of indazole in a mixture of 3 ml of dry pyridine and 40 ml of benzene. The reaction mixture was stirred at the same temperature for 6 hr. Then the precipitate of pyridine hydrochloride was filtered, the benzene solution was evaporated to dryness in vacuo at room tempera-ture, and the residue was dried in a vacuum desiccator over sulfuric acid. We obtained 2 g of compound with m.p. 121 — 125°. The compound was dissolved in 80 ml of dry benzene, the small amount of benzene-insoluble isonicotinoyl chloride hydrochloride removed by filtration, and the benzene solution was treated with a small amount of carbon and then allowed to stand overnight. The next day the carbon was removed, the solution was evaporated in vacuo at room temperature to a volume of serveral milliliters, and the obtained precipitate was filtered and dried in a vacuum. The obtained compound, m.p. 126 — 128°, was treated with absolute ether. Here we obtained the pure 2-isonicotinoylindazole with m.p. 131 — 131.5°, while the mixed melting point with the 1-isomer was 110-140°. Colorless needles, readily soluble in mineral acids, and more difficulty soluble in alco-hol, benzene,and ether. When heated above its melting point, 2-isonicotinoylindazole is converted to a substance with m.p. 139°, which fails to depress the melting point when mixed with 1-isonicotinoylindazole.

Found %: C 69.89; H 4.09; N 18.63. $C_{13}H_9ON_3$. Calculated %: C 69.94; H 4.06; N 18.83.

1-Isonicotinoyl-3-chloroindazole was synthesized in the same manner as 1-isonicotinoylindazole. Yield 90%.

1-Isonicotinoyl-3-chloroindazole was obtained from alcohol as long colorless needles, m.p. 142 — 142.5°, readily soluble in chloroform, dichloroethane, glacial acetic acid,and mineral acids, more difficulty soluble in ethyl acetate, benzene and alcohol, and difficulty soluble in ether.

Found %: C 60.42; H 2.94; N 16.54; Cl 13.68, 13.84. $C_{13}H_8ON_3Cl$. Calculated %: C 60.59; H 3.13; N 16.31; Cl 13.77.

Treatment of 0.1 g of 1-isonicotinoyl-3-chloroindazole with 4 ml of 5% hydrochloric acid gave the hydro-chloride as colorless prisms. The filtrate, after removal of the hydrochloride, on standing for several minutes gave a precipitate with m.p. 148°, which failed to depress the melting point when mixed with 3-chloroindazole. Treatment of 1-isonicotinoyl-3-chloroindazole hydrochloride with sodium carbonate solution gave the starting acyl derivative of 3-chloroindazole with m.p. 140-141°, failing to depress the melting point when mixed with the pure specimen.

1-Isonicotinoyl-6-isonicotinoyloxyindazole. To a suspension of isonicotinoyl chloride hydrochloride (obtained from 6.15 g of isonicotinic acid) in 20 ml of dry benzene was gradually added, with stirring, 2.68 g of finely ground 6-hydroxyindazole in a mixture of 30 ml of dry benzene and 8 ml of dry pyridine. The reaction mixture was heated in a glycerin bath at 80-85° for 5 hr. After working up the reaction mass in the same manner as described for the preparation of 1-isonicotinoylindazole, we obtained 3.76 g of a colorless compound with m.p. 178 — 179°. After two recrystallizations from alcohol the 1-isonicotinoyl-6-isonicotinoyloxyindazole had m.p. 184 — 185.5°; colorless prisms, readily soluble in mineral acids, chloroform, dichloroethane,and glacial acetic acid, more difficultly soluble in alcohol, benzene,and ethyl acetate, and difficulty soluble in ether.

Found %: C 66.18; H 3.42; N 16.47. $C_{19}H_{12}O_3N_4$. Calculated %: C 66.28; H 3.51; N 16.27.

A solution of 0.1 g of 1-isonicotinoyl-6-isonicotinoyloxyindazole in 0.5 ml of 5% hydrochloric acid was allowed to stand for 5 min, after which it was neutralized with sodium carbonate solution, and the obtained pre-cipitate was filtered, washed with water, and dried. The obtained compound had m.p. 182°, and failed to depress the melting point when mixed with the original free base.

1-Isonicotinoyl-6-acetamidoindazole was synthesized in the same manner as 1-isonicotinoylindazole. 1-Isonicotinoyl-6-acetamidoinadazole was obtained as long colorless needles with m.p. 251 − 252°, readily soluble in glacial acetic acid and pyridine, more difficultly soluble in acetone, alcohol, and ethyl acetate, and almost insoluble in ether.

Found %: C 64.35; H 4.36; N 19.82. $C_{15}H_{12}O_2N_4$. Calculated %: C 64.28; H 4.32; N 19.99.

The trituration of 0.05 g of 1-isonicotinoyl-6-acetamidoindazole with 2 ml of 5% hydrochloric acid gave the hydrochloride. Treatment of the hydrochloride with sodium carbonate solution in the cold gave the starting acyl derivative of 6-acetamidoindazole, which had m.p. 251°, and failed to depress the melting point when mixed with the pure specimen.

1-Isonicotinoyl-6-nitroindazole. To a suspension of isonicotinoyl chloride hydrochloride (prepared from 1.02 g of isonicotinic acid and 8 ml of thionyl chloride) in 15 ml of dry pyridine was added 1.22 g of 6-nitroindazole, in portions, with stirring. The mixture was heated at 100 − 110° for 4 hr. The reaction mass was worked up the same as in the preceding experiment. We obtained 1.71 g of substance with m.p. 201 − 204°. Two recrystallizations from alcohol gave 1-isonicotinoyl-6-nitroindazole as fine colorless needles with m.p. 214 − 215°, readily soluble in acetone, chloroform, and mineral acids, more difficultly soluble in alcohol and benzene, and very difficulty soluble in ether.

Found %: C 58.01, 58.08; H 3.07, 2.93; N 20.94. $C_{13}H_8O_3N_4$. Calculated %: C 58.21; H 3.01; N 20.89.

A mixture of 0.1 g of 1-isonicotinoyl-6-nitroindazole and 3 ml of dry quinoline was refluxed for 45 min. After cooling, the mixture was diluted with petroleum ether, and the obtained precipitate was filtered, washed with petroleum ether, and dried. The obtained substance had m.p. 213 − 214°; the mixed melting point with 1-isonicotinoyl-6-nitroindazole, obtained as described above, was not depressed.

A solution of 0.1 g of 1-isonicotinoyl-6-nitroindazole in 35 ml of 5% hydrochloric acid was cooled efficiently, and then made alkaline with sodium carbonate. The obtained precipitate was filtered and washed, first with sodium carbonate solution, and then with water. The obtained substance had m.p. 178°, and failed to depress the melting point when mixed with 6-nitroindazole.

1-Nicotinoyl-6-nitroindazole was obtained in the same manner as 1-isonicotinoyl-6-nitroindazole. Two recrystallizations from benzene gave 6-nitro-1-nicotinoylindazole as colorless needles with m.p. 173 − 174°, readily soluble in acetone and dilute mineral acids, more difficulty soluble in alcohol and benzene, and insoluble in water.

Found %: C 58.51; H 3.01; N 20.95, 20.90. $C_{13}H_8O_3N_4$. Calculated %: C 58.21; H 3.01; N 20.89.

1-(p-Nitrobenzoyl)-6-nitroindazole was synthesized in the same manner as 1-isonicotinoyl-6-nitroindazole. 1-(p-Nitrobenzoyl)-6-nitroindazole was obtained as long colorless needles (from acetone) with m.p. 234 − 235°, soluble in hot ethyl acetate and hot chloroform, more difficulty soluble in acetone, methyl alcohol, and ethyl alcohol, and almost insoluble in ether.

Found %: C 53.83; H 2.49; N 18.10. $C_{14}H_8O_5N_4$. Calculated %: C 53.85; H 2.58; N 17.95.

SUMMARY

1. We synthesized the 1- and 2-isonicotinoylindazoles, and a number of their 3- and 6-substituted derivatives.

2. It was shown that 2-isonicotinoylindazole rearranges to 1-isonicotinoylindazole when heated above its melting point.

3. It was shown that a substituent in the indazole ring affects the stability of the N − C bond between the indazole ring and the acyl group.

LITERATURE CITED

[1] M. N. Shchukina, G. N. Pershin, and co-workers, Proc. Acad. Sci. USSR 84, 981 (1952); M. N. Shchukina, G. N. Pershin, and co-workers, Collection: Chemistry and Medicine , Phthivazide [in Russian] (State Press of Medical Literature, Moscow, 1954), pp. 12 − 25; J. J. D. Hart, G. Rutherford, and co-workers, Antibiotics and Chemotherapy 4, 803 (1954).

[2] K. von Auwers and M. Düesberg, Ber. 53, 1179 (1920).

[3] K. von Auwers, Ber. 52, 1330 (1919).

[4] K. von Auwers and H. G. Allardt, Ann. 438, 1 (1924).

[5] M. N. Shchukina and E. D. Sazonova, J. Gen. Chem., Suppl. II, 1081 (1953).

[6] H. H. Fox and J. T. Gibas, J. Org. Chem. 20, 60 (1955); I. Ya. Postovskii and N. N. Vereshchagina, Proc. Acad. Sci. USSR 110, 802 (1956).*

[7] E. Sorkin, W. Roth, and H. Erlenmeyer, Helv. Chim. Acta, 35, 1736 (1952); S. Fallab and H. Erlenmeyer, Experientia 8, 298 (1952); J. Cymerman-Craig, D. Willis, S. D. Rubbo, and J. Edgar, Nature 176, 34 (1955).

Received November 24, 1958

---

*Original Russian pagination. See C. B. Translation.

# INVESTIGATIONS IN N-SUBSTITUTED INDAZOLE SERIES

III. SYNTHESIS OF N-THIOCARBAMOYL DERIVATIVES OF INDAZOLE*

Jao Êrh-Ch'ang and M. N. Shchukina

S. Ordzhonikidze All-Union ChemicalPharmaceutical Scientific Research Institute

The thiocarbamoyl derivatives of indazole can be regarded as cyclized aromatic thiosemicarbazones or as substituted thioureas. Since highly active antitubercular compounds [1] belong to these two classes of compounds, it seemed to interest to synthesize compounds of a similar type for testing as antibacterials.

Of the thiocarbamoyl compounds in the indazole series only the phenylthiocarbamoylindazole [2] is known, obtained by heating indazole with phenyl isothiocyanate. We used different methods to synthesize the thiocarbamoylindazoles, substituted in the indazole ring and also on the nitrogen of the thiocarbamoyl radical. Thus, N-thiocarbamoyl-6-hydroxyindazole (I) was obtained in low yield by heating 6-hydroxyindazole with ammonium thiocyanate in chlorobenzene medium, with the simultaneous passage of a stream of hydrogen chloride.
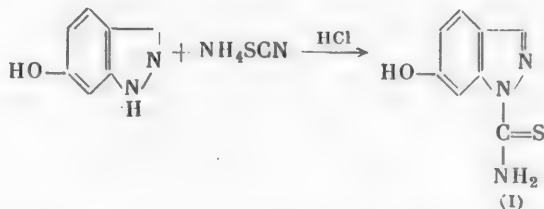

Only the primary amino group in 6-aminoindazole reacts with ammonium thocyanate, and even employing a large excess of ammonium thiocyanate gave us only N-(6-indazolyl)thiourea (II).

Reaction failed to go when we heated 6-nitroindazole with ammonium thiocyanate under various conditions, and only the starting 6-nitroindazole was isolated from the reaction mixture. The heating of 6-nitroindazole with phenyl isothiocyanate or with acetyl isothiocyanate also failed to yield the corresponding thiocarbamoyl derivatives. Indazole itself also fails to react with ammonium thiocyanate, but it does react with phenyl isothiocyanate.

A general method for obtaining N-thiocarbamoyl derivatives of indazole was found in the reaction of thiophosgene [3, 4] with indazole and its derivatives, followed by reacting the indazolylthiocarbamoyl chlorides obtained in this manner with either ammonia or primary and secondary amines.

The reaction of the indazole with thiophosgene was run in dry ether with cooling, using pyridine as the condensation agent. To obtain the thiocarbamoyl derivatives, we took the thus formed indazolylthiocarbonyl chloride in ether solution, without isolation, and reacted it with ether excess ammonia or amines. Reaction with ammonia gave the thiocarbamoylindazole (III), while reaction with piperidine gave 1(2)-(N-piperidyl)-thiocarbamoylindazole (IV).

---

* Communication II: see J. Gen. Chem. **29**, 3720 (1959).
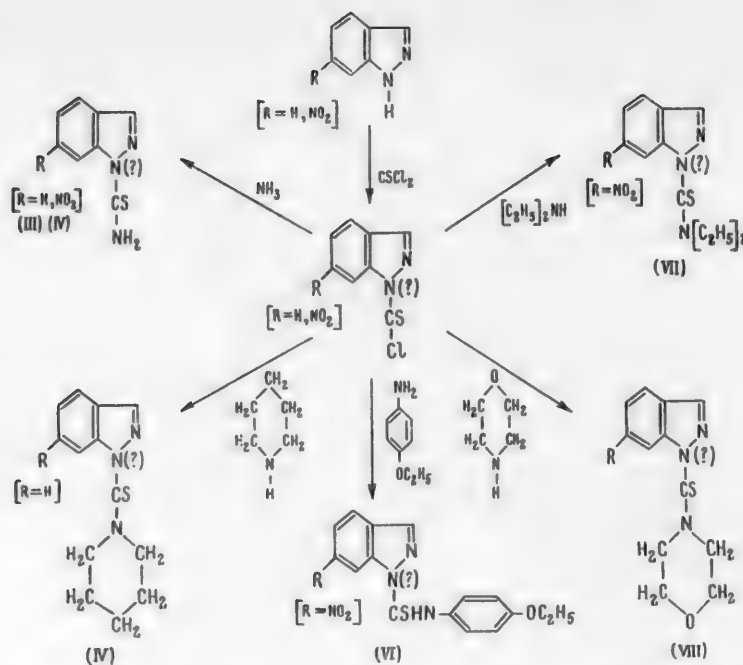
To obtain N-(6-nitroindazolyl)thiocarbonyl chloride it proved necessary to heat 6-nitroindazole with a large excess of thiophosgene in benzene at 55-65˙. The condensation agent used in this case was triethylamine. The condensation of 6-nitroindazolylthiocarbonyl chloride with ammonia or the proper amine gave us the four thiocarbamoyl derivatives of 6-nitroindazole, (V), (VI), (VII) and (VIII).

We were unable to prove fully the structure of the obtained thiocarbamoyl derivatives, either of the 1- or the 2-substituted derivatives; however, by analogy with the carbamoyl derivatives of indazole described in [5], it is possible to assume that the compounds synthesized by us are the 1-substituted derivatives. When they were heated, in not a single case was their transition to the more stable isomer observed, as was described for the 2-carbamoyl derivatives, which undergo rearrangement to the 1-isomers when heated.

In the course of synthesizing the thiocarbamoyl derivatives we observed that a relationship exists between the stability of these compounds and the substituent found in the indazole ring, and also in the thiocarbamoyl radical. Both N-thiocarbamoylindazole and N-thiocarbamoyl-6-nitroindazole are very unstable: even when recrystallized from a low-boiling solvent (for example, benzene or alcohol), they decompose with the formation of the corresponding indazoles. A hydroxyl group in the 6 position substantially enhances the stability of the bond between the indazole nucleus and the thiocarbamoyl group: N-thiocarbamoyl-6-hydroxyindazole is obtained at 110-120°, and can be recrystallized from boiling water.

Phenylthiocarbamoylindazole can be recrystallized from alcohol, whereas p-ethoxyphenylthiocarbamoyl-6-nitroindazole, when recrystallized from alcohol, decomposes into 6-nitroindazole and p-ethoxyphenyl isothiocyanate. The instability of this compound is apparently due to the presence of a nitro group in the 6 position of the indazole nucleus. N,N-Disubstituted derivatives of thiocarbamoylindazole are more stable than the compounds having an unsubstituted amino group in the thiocarbamoyl radical. Derivatives with one substituent on the nitrogen in the thiocarbamoyl group occupy an intermediate position in this respect. The instability shown by the N-monosubstituted and unsubstituted thiocarbamoyl derivatives of indazole and 6-nitroindazole explains why we were unable to obtain the thiocarbamoyl derivatives of indazole and 6-nitroindazole, either by heating the latter compounds with ammonium or potassium thiocyanate in an acid medium, or by heating 6-nitroindazole with phenyl isothiocyanate.

The compounds obtained by us were tested for their antibacterial action.* 1(2)-Thiocarbamoyl-6-hydroxy-indazole has a quite high tuberculostatic action and inhibits the growth of the human strain of tubercle bacillus at

---

*The testing was done in the Division of Chemotherapy of the All-Union Chemical-Pharmaceutical Scientific Research Institute under the supervision of G. N. Pershin, for which the authors wish to thank him.

a dilution of 1:256,000; 1(2)-phenylthio-carbamoylindazole is somewhat less active (the maximum tuberculostatic dilution is 1:128,000).

EXPERIMENTAL

1(2)-Thiocarbamoyl-6-hydroxyindazole (I). A stream of dry hydrogen chloride was passed for 10 min , at 110-120°, with stirring, into a mixture of 1.34 g of finely ground 6-hydroxyindazole and 0.91 g of dry powdered ammonium thiocyanate in 15 ml of chlorobenzene. Then the mixture was heated at the same temperature for 4 hr. During this time a stream of dry hydrogen chloride was passed through the mixture for 10 min at 20 min intervals. The chlorobenzene was vacuum distilled, and the residue was heated with 15 ml of water at the boil. After cooling, the product was filtered and dried. We obtained 0.23 g (11.9%) of substance with m.p. 166-169°. Two recrystallizations from water gave 1(2)-thiocarbamoyl-6-hydroxyindazole as colorless needles with m.p. 169.5-170.5°, readily soluble in acetone, alcohol,and hot water, and difficultly soluble in cold water.

Found %: C 49.81, 49.84; H 4.00, 3.76; N 21.67; S 16.22. $C_8H_7ON_3S$. Calculated %: C 49.73; H 3.65; N 21.75; S 16.59.

Neutralization of the water filtrate with ammonia gave 0.71 g of starting 6-hydroxyindazole.

N-(6-Indazolyl)thiourea (II). a) To a solution of 6.65 g of 6-aminoindazole in 40 ml of water and 6 ml of concd. hydrochloric acid was added, with stirring, 4.1 g of ammonium thiocyanate in 5 ml of water. The mixture was heated on the water bath for 1 hr, allowed to stand for 1 hr at room temperature, and then it was evaporated slowly to dryness. The residue was triturated with 40 ml of water, and the mixture was again slowly evaporated to dryness on the water bath. The residual yellow substance was heated for another 5 hr, after which the residue was ground and slowly heated with 25 ml of water to 70° with stirring. After cooling to 35°, the crystalline substance was filtered, washed with 30 ml of cold water, and dried. We obtained 7.8 g of substance with m.p. 189-190° (decompn.). N-(6-Indazolyl)thiourea was obtained as colorless prisms (from 50% aqueous alcohol) with m.p. 190-191° (decompn.), soluble in acetone and hot alcohol, difficultly soluble in hydrochloric acid, and very difficultly soluble in benzene, ether, and chloroform. The substance fails to give a positive isonitrile test, characteristic for primary amines.

Found %: C 50.01; H 4.26; N 29.21; S 16.65. $C_8H_8N_4S$. Calculated %: C 49.98; H 4.19; N 29.15; S 16.68.

b) A mixture of 6.65 g of 6-aminoindazole. 9.12 g of ammonium thiocyanate, 30 ml of glacial acetic acid and 2.5 ml of water was heated at 80-95° for 6 hr. The obtained precipitate was filtered, washed with cold water, and dried. We obtained 4.88 g of yellow compound with m.p. 189° (decompn.); after two recrystallizations the compound had m.p. 191° (decompn.), and did not depress the melting point when mixed with the specimen obtained by method a.

The acetic acid filtrate was heated for another 10 hr at 120°. After cooling, the obtained precipitate was filtered, washed with water, and dried. We obtained 1.66 g of yellow compound; after recrystallization from alcohol this compound had m.p. 243-245°, which corresponds to the literature data for 6-acetamidoindazole. The mixed melting point with an authentic specimen was not depressed.

1(2)-Thiocarbamoylindazole (III). To a solution of 2.3 g (1.52 ml) of thiophosgene in 50 ml of absolute ether was added, with stirring, at -5 to 0°, in drops, over a period of 1.5 hr, a solution of 2.36 g of indazole and 1.58 g of dry pyridine in 150 ml of absolute ether, after which the reaction mass was stirred at room temperature for another 0.5 hr. The obtained precipitate was filtered and washed with dry ether. With stirring and ice cooling, a stream of dry ammonia was passed through the ether solution for 30 min, after which the mixture was stirred at room temperature for another 0.5 hr. The precipitate of ammonium chloride was filtered and washed with ether, and the ether solution was evaporated to dryness in vacuo to give 2.94 g (83.1%) of light-yellow compound with m.p. 81-83°. For analysis, the specimen was purified by recrystallization from ether. Colorless prisms with m.p. 87-87.5°, readily soluble in alcohol and acetone.

Found %: C 54.41; H 4.13; N 23.56. $C_8H_7N_3S$. Calculated %: C 54.22; H 3.98; N 23.71.

<u>1(2)-(N-Piperidyl)thiocarbonylindazole (IV)</u>. To an ether solution of N-indazolylthiocarbonyl chloride (prepared from 2.3 g of thiophosgene and 2.36 g of indazole by the above described method) was added, with stirring and ice cooling, in drops, a solution of 3.42 g of dry piperidine in 10 ml of absolute ether, after which the reaction mixture was stirred for another hour at room temperature. After removal of the precipitate of piperidine hydrochloride, the ether solution was evaporated. We obtained 4.3 g of a mixture of yellow crystals and an oil. This mixture was treated with a small amount of absolute ether, and the precipitate was filtered. We obtained 1.56 g of yellow substance with m.p. 99-103°. After two recrystallizations from alcohol, m.p. 103-103.5°. 1(2)-(N-Piperidyl)thiocarbamoylindazole was obtained as light-yellow prisms, readily soluble in ether, chloroform ,and benzene, and moderately soluble in alcohol.

Found%: C 63.69; H 6.03; N 17.43; S 13.00, 13.15. $C_{13}H_{15}N_3S$. Calculated %: C 63.64; H 6.16; N 17.13; S 13.07.

Evaporation of the ether mother liquor gave a viscous brown-yellow oil, which failed to crystallize even when allowed to stand for a long time. The oil distilled at 118° (0.01 mm), but most of it decomposed during the distillation. A small amount of substance with m.p. 144-145° was isolated from the distillate, which proved to be indazole.

<u>1(2)-Thiocarbamoyl-6-nitroindazole (V)</u>. To a solution of 2.3 g of thiophosgene in 50 ml of anhydrous benzene was added, with stirring, at 55-65°, in 2 hr, a solution of 1.63 g of 6-nitroindazole in 320 ml of anhydrous benzene and 1.11 g of triethylamine. The stirring was continued at the same temperature for another 2.5 hr. The precipitate of triethylamine hydrochloride was filtered. The filtrate was evaporated in vacuo to dryness. To remove the thiophosgene completely, the residue was treated with 60 ml of anhydrous benzene, and the mixture again evaporated to dryness. A stream of dry ammonia was passed for 45 min, with stirring, at -14 to -10°, into a solution of the obtained N-(6-nitroindazolyl) thiocarbonyl chloride in 160 ml of dry toluene, after which the mixture was stirred at the same temperature for another hour. The obtained precipitate was filtered (6-nitroindazole was isolated from the toluene filtrate); the precipitate was washed with a little dry benzene and then dissolved in 40 ml of acetone. After removal of the ammonium chloride, the solution was decolorized with carbon and then evaporated in vacuo at room temperature to a volume of 3 ml, after which the obtained precipitate was filtered and dried in vacuo. The obtained light-yellow substance had m.p. 182-184° (decompn.). 1(2)-Thiocarbamoyl-6-nitroindazole was obtained as light-yellow prisms, readily soluble in acetone, and more difficultly soluble in alcohol, benzene, chloroform, and ether.

Found %: C 43.69; H 2.91; N 25.18, 25.22; S 14.50. $C_8H_6O_2N_4S$. Calculated %: C 43.24; H 2.72; N 25.21; S 14.43.

<u>1(2)-(p-Ethoxyphenyl)thiocarbamoyl-6-nitroindazole (VI)</u>. To a solution of N-(6-nitroindazolyl)thiocarbonyl chloride (prepared from 2.3 g of thiophosgene and 1.63 g of 6-nitroindazole by the method described in the preceding experiment) in 130 ml of anhydrous benzene was added, with stirring, at room temperature, in 50 min, a solution of 2.74 g of freshly distilled p-phenetidine in 30 ml of anhydrous benzene. Then the reaction mixture was stirred for another 3.5 hr. When reaction was done, the precipitate of p-phenetidine hydrochloride was filtered and washed with 20 ml of dry benzene. The combined solution was vacuum evaporated in the cold to dryness, and the residue was washed with 37 ml of anhydrous alcohol. The residual yellow substance (0.57 g), after drying in vacuo, had m.p. 129-132°. The substance was dissolved in 145 ml of benzene and treated with carbon; the solution was evaporated in vacuo at room temperature to a volume of about 8 ml, and the obtained precipitate was filtered and vaccum dried. 1(2)-(p-Ethoxyphenyl) thiocarbamoyl-6-nitroindazole was obtained as yellow prisms with m.p. 132-133°, readily soluble in acetone and alcohol, and more difficultly soluble in benzene.

Found %: C 56.36; H 3.95; N 16.26. $C_{16}H_{14}O_3N_4S$. Calculated %: C 56.13; H 4.12; N 16.37.

The alcohol solution from washing the reaction product was vacuum evaporated in the cold, the residue was washed with a little ether, the ether removed by evaporation, and after two recrystallizations from benzene we obtained a light-yellow substance with m.p. 181°, which was identified as being starting material. The ether-insoluble portion of the substance was identified as being p-ethoxyphenyl isothiocyanate.

<u>1(2)-(Diethylthiocarbamoyl)-6-nitroindazole (VII)</u> was obtained in the same manner as 1(2)-(p-ethoxyphenyl)-thiocarbamoyl-6-nitroindazole. 6-Nitro-1(2)-(diethylthiocarbamoyl)indazole was obtained as light-yellow prisms (from a mixture of alcohol and benzene), m.p. 155-156°. The compound is readily soluble in chloroform and acetone, moderately soluble in alcohol, benzene,and ethyl acetate, and insoluble in ether.

Found %: C 51.96; H 5.26; N 19.87; S 11.09. $C_{12}H_{14}O_2N_4S$. Calculated %: C 51.78; H 5.07; N 20.13; S 11.52.

1(2)-(N-Morpholinyl)thiocarbony—6-nitroindazole (VIII) was synthesized in the same manner as 1(2)-
(p-ethoxyphenyl)thiocarbamoyl-6-nitroindazole. Recrystallization from a mixture of benzene and ethyl acetate
gave 1(2)-(N-morpholinyl)thiocarbonyl-6-nitroindazole as yellow prisms with m.p. 203-204°, readily soluble
in chloroform and dichloroethane, moderately soluble in alcohol, ethyl acetate,and acetone, and difficulty
soluble in benzene and ether.

Found %: C 49.59; H 3.99; N 19.11; S 10.91. $C_{12}H_{12}O_3N_4S$. Calculated %: C 49.31; H 4.14; N 19.17; S 10.97.

SUMMARY

A number of N-thiocarbamoyl derivatives of indazole were synthesized. A general method for their pre-
paration is the reaction of indazole and its 6-substituted derivatives with thiophosgene, followed by treatment of
the obtained indazolythiocarbonyl chlorides with ammonia, or with primary and secondary amines. N-Thio-
carbamoyl-6-hydroxyindazole was obtained by heating 6-hydroxyindazole with ammonium thiocyanate. Only
the primary amino group in 6-aminoindazole reacts under these conditions, yielding N-(6-indazolyl)thiourea.

It was found that the synthesized N-thiocarbamoyl derivatives of indazole do not rearrange when heated,
and apparently are the 1-substituted derivatives.

It was established that the stability of the bond between the indazole nucleus and the thiocarbamoyl radical
depends on the nature of the substituents in the indazole ring and on the nitrogen of the thiocarbamoyl radical.

LITERATURE CITED

[1] M. N. Shchukina and T. P. Sycheva, Chemical Science and Industry [USSR] 1, 419 (1956).

[2] K. von Auwers and H. Kleiner, J.prakt. Chem. 118, 67 (1928).

[3] O. B. Helfrich and E. E. Reid, J. Am. Chem. Soc. 43, 591 (1921).

[4] G. M. Dyson, F. C. Whitmore, and A. M. Griswold, Org. synt. 2d ed. N. Y. (1949); Coll. vol. I, 506.

[5] K. von Auwers and E. Frese, Ann. 450, 273 (1926).

# CHEMICAL TRANSFORMATIONS OF α-HALO KETONES

VII. CHARACTERISTICS OF DIOXANE DIBROMIDE AS A BROMINATION AGENT

T. I. Temnikova and N. A. Oshueva

Leningrad State University

Of the different methods for the halogenation of carbonyl-containing organic compounds, the mildest is the bromination technique using dioxane dibromide, developed by L. A. Yanovskaya and A. P. Terent'ev [1]. With this method it is possible to obtain, in good yield, quite unstable α-bromo aldehydes and α-bromo ketones, for example, α-bromocyclohexanone [1, 2]. In their paper, Yanovskaya and Terent'ev brominated aldehydes and, with the exception of menthone, only those ketones that could yield only the monobromo derivative. (The structure of monobromomenthone was not established). As a result, the manner in which dioxane dibromide functions as a brominating agent was not determined.

As a continuation of our previous investigation [2], it seemed of interest to obtain 1-bromo-1-methyl-2-cyclohexanone (II).
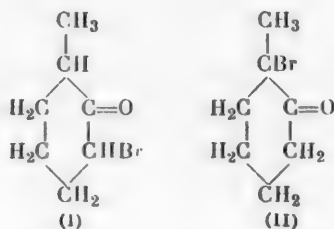
An unequivocal method for the preparation of 1-bromo-1-methyl-2-cyclohexanone is not reported in the literature. Kotz [3] assumed that the product obtained by the direct bromination of 1-methyl-2-cyclohexanone with bromine vapors in a carbon dioxide stream is 3-bromo-1-methyl-2-cyclohexanone (I). According to Kotz, the chlorination goes in a similar manner and yields 3-chloro-1-methyl-2-cyclohexanone. Godchot and Bedos [4] repeated the experiment of Kotz on the chlorination of 1-methyl-2-cyclohexanone, but they obtained an α-chloro ketone with different constants. On the basis of subsequent transformations of the compound they decided that they had 1-chloro-1-methyl-2-cyclohexanone. Corey and co-workers [5], employing the Kotz procedure, obtained a bromomethylcyclohexanone with b.p. 52° (2 mm), which, in their opinion, was the tertiary bromo ketone (II). However, they failed to given proof of the structure, apparently assuming that the bromination went in the same manner as the chlorination, described earlier [4].

When we used dioxane dibromide to brominate 1-methyl-2-cyclohexanone, we isolated a fraction of bromo ketones that boiled in the range 72-78° (8-10 mm). Further separation of this fraction by fractional distillation proved impossible, and it was decided to establish the structure of the bromo ketones through their hydrolysis products. Since the direct hydrolysis of bromo ketones goes with difficulty (incomplete hydrolysis, tarring, oxidation of the hydrolysis products), we made use of the ability of bromo ketones to undergo rapid and practically complete conversion to ketals, which hydrolyze with ease.

As the result of hydrolyzing the unstable methyl phenyl ketal of α-methylcyclohexanone we obtained a mixture of keto alcohols, containing 70% of the secondary keto alcohol, 1-methyl-2-cyclohexanon-3-ol, and 30% of the tertiary keto alcohol, 1-methyl-2-cyclohexanon-1-ol. In this way it was established that it was the hydrogen on the least hydrogenated carbon atom that was mainly replaced by bromine.

In connection with this it was interesting to determine if the bromination of unsymmetrically substituted ketones of the aliphatic series with dioxane dibromide would go in a similar manner. For this we investigated the bromination of methyl isopropyl ketone. In this case also we isolated a mixture of isomeric bromides, which we were unable to separate by fractional distillation in vacuo; the mixture analyzed as approximately 75% of the tertiary bromide and about 25% of the primary bromide. The bromination of methyl isopropyl ketone in water solution in the presence of $KClO_3$ gives the bromo ketones in the same proportion [6].

On the basis of our data it must be assumed that dioxane dibromide cannot be used to brominate ketones with dynamically unequal α-positions. The process goes simultaneously in two directions, and which bromo ketone predominates in the bromination mixture depends on the structure of the starting ketone. As a result, bromination with dioxane dibromide goes in the same manner as does the bromination of ketones with bromine in the presence of bases [6].

EXPERIMENTAL

I. Reaction of Dioxane Dibromide with 1-Methyl-2-cyclohexanone According to the Yanovskaya and Terent'ev Method [1]

Bromination. Dioxane dibromide (85 g) was added with vigorous stirring to 35 g of 1-methyl-2-cyclohexanone, dissolved in a mixture of 33 ml of dioxane and 160 ml of ether. The ether-ketone layer was washed well with water, and then it was dried over magnesium sulfate. The solvent was then distilled off, and the bromo ketone was vacuum distilled in a stream of nitrogen. Yield 30 g. B.p. 72-78° (8-10 mm).

Preparation of methyl phenyl ketals of 1-methyl-2-cyclohexanonol. To a solution of sodium phenolate, prepared by dissolving 2.41 g of sodium in 40 ml of methyl alcohol and then adding 9.9 g of phenol, was added 20 g of the bromomethylcyclohexanone with b.p. 72-78° (8-10 mm). The sodium bromide precipitate was filtered, while the filtrate of mixed ketals was washed with alkali to remove traces of phenol, and then it was vacuum distilled. B.p. 57-61° (5-6 mm). Yield 18 g. The mixture of ketals reduced Fehling solution, i.e., it is readily hydrolyzed.

Hydrolysis of mixed methyl phenyl ketals. Two grams of the product was hydrolyzed with 30 ml of 5% H_2SO_4 in the presence of 7 ml of alcohol. The mixture was heated under reflux for 2 hr, after which it was saturated with potassium carbonate, the keto alcohol extracted from the weakly alkaline solution with ether, the solvent distilled off, and the residue was vacuum distilled. B.p. 58-59° (5 mm).

Quantitative determination of the amount of secondary keto alcohol [7]. Into each of two Erlenmeyer flasks was charged 10 ml of an alkaline solution of potassium sodium tartrate, 10 ml of a copper sulfate solution (69.28 g in 1 liter), and 20 ml of water. An ampule containing the substance was placed in one of the flasks. The flasks were heated for 10 min under reflux, after which they were cooled, and to each was added 10 ml of 30% KI solution and 10 ml of 25% H_2SO_4. The liberated iodine was titrated with 0.1N thiosulfate solution, and the amount of iodine liberated in the blank experiment was substracted. The amount of secondary α-keto alcohol was found to be 63.5%

Then the degree of change suffered by the keto alcohol in alkaline medium was determined. For this the weighed sample was first boiled for 10 min in potassium sodium tartrate solution, and then 10 ml of copper sulfate solution was added, and the determination run in the same manner as described above. The amount of secondary α-keto alcohol was found to be 54.6%.

Consequently, taking into consideration the degree of change suffered by the secondary α-keto alcohol in alkaline medium, the mixture contained about 70% of 1-methyl-2-cyclohexanon-3-ol.

II. Reaction of Dioxane Dibromide with Methyl Isopropyl Ketone

Ninety grams of dioxane dibromide was added as rapidly as decolorization occurred to 30 g of the ketone, dissolved in a mixture of 30 ml of dioxane and 120 ml of absolute ether. The manner in which the bromination went was described above. Fractional distillation of the bromination mixture yielded two fractions, corresponding to the isomeric α-bromo ketones: 27.3 g with b.p. 54-55° (50 mm), and 8.3 g with b.p. 83-84° (46 mm); the 1st fraction was the tertiary bromide (from the literature: b.p. 49° at 22 mm [8], and 78° at 100 mm [6]); and the 2nd fraction was the primary bromide (from the literature [9]: b.p. 86° at 50 mm).

Using the A. E. Favorskii method [8], the tertiary bromide was converted to the semicarbazone of dimethylacetylcarbinol, m.p. 164°, which agrees with the literature data [8]. Reaction of the tertiary bromide with sodium methylate in methyl alcohol gave the dimethyl ketal, which (without isolation in the pure state) was hydrolyzed. The hydrolysis product was dimethylacetylcarbinol with b.p. 46-47° (14 mm) (literature data: 50° at 18 mm).

The primary bromide was oxidized with the calculated amount of alkaline bromine liquor, and the pure acid was isolated from the obtained salt: b.p. 52° (9 mm), n_D^{20} 1.3957, neutralization equivalent 92. These data correspond to isobutyric acid (b.p. 154°, n_D^{20} 1.3930, neutralization equivalent 88).

SUMMARY

It was shown that the use of dioxane dibromide to brominate ketones with dynamically unequal α-positions goes with the formation of a mixture of isomeric α-bromo ketones, i. e. the reaction goes in the same manner as when bromination is in the presence of a base.

LITERATURE CITED

[1] L. A. Yanovskaya and A. P. Terent'ev, J. Gen. Chem. 22, 1598 (1952).*

[2] T. I. Temnikova and N. A. Oshueva, J. Gen. Chem. 18, 2224 (1958). *

[3] A. Kötz and H. Steinhorst, Ann. 379, 1 (1911).

[4] M. Godchot and P. Bedos, C. r. 181, 919 (1925).

[5] E. G. Corey, T. H. Topie, and W. A. Wozniak, J. Am. Chem. Soc. 77, 5415 (1955).

[6] H. M. E. Cardwell and A. E. H. Kilner, J. Chem. Soc. 2430 (1951).

[7] T. I. Temnikova and V. A. Kropachev, J. Gen. Chem. 19, 2069 (1949).*

[8] A. E. Favorskii and A. A. Vansheidt, J. Russ. Chem. Soc. 44, 1358 (1912).

[9] J. R. Catch, D. F. Elliott, D. H. Hey, and E. R. H. Jones, J. Chem. Soc. 278 (1948).

* Original Russian pagination. See C. B. Translation.

CONJUGATED SYSTEMS

CVIII.* SYNTHESIS AND PROPERTIES OF SOME ALKYISOALKENYLACETYLENES AND HIGHER HOMOLOGS OF VINYLALKYLACETYLENES

A. A. Petrov, B. S. Kupin, T. V. Yakovleva
and K. S. Mingaleva
Lensovet Leningrad Technological Institute

In order to make a systematic study of the relation between structure, physical properties, and reactivity in the relation between structure, physical properties, and reactivity in the vinylacetylenic hydrocarbon series, it was necessary for us to have some of the higher vinylalkylacetylenes and 1,3-dialkyl-substituted derivatives of vinyl-acetylene. We were able to synthesize these compounds by reacting the proper halo derivatives with the sodium derivatives of vinylacetylene and isoalkenylacetylenes in liquid ammonia. The higher vinylalkylacetylenes were obtained earlier using both this and other methods [1,2]. Except for 2-methyl-1-penten-3-yne [3, 4], the dialkyl-vinylacetylenes are new compounds. The constants of the obtained hydrocarbons are given in Table 1.

The dipole moments were measured for the three hydrocarbons given in Table 2. The dipole moments of the other vinylacetylenic hydrocarbons reported here were measured earlier [5]. A comparison of the dipole moments of these hydrocarbons with the moments of the corresponding alkylvinylacetylenes and isoalkenylacetylenes reveals that substitution in the 1 and 3 positions increases the polarity of the hydrocarbon when compared with the hydrocarbons in which each of these positions is substituted separately. This can be explained on the assumption that the electrons in these compounds are shifted toward the double bond.

The infrared spectra of the vinylalkylacetylenes and isoalkenylalkylacetylenes described in this paper are shown in the figure. All of the rules observed earlier for the spectra of the lower vinylalkylacetylenes [6] also apply to the higher homologs.

The conjugated double bond is shown in the spectra by an intense absorption at 1610 cm^{-1}, which is somewhat lower than the frequency for olefins, while the acetylenic bond is shown by an absorption at 2228 cm^{-1}.† Both absorptions are accompanied by weak bands at lower values (1588 and 2183 cm^{-1}, respectively). An absorption at 1640 cm^{-1} also indicates the presence of the acetylenic grouping.

The vinyl group is characterized by three absorption bands due to the valence vibrations (3100, 3045 and 3012 cm^{-1}), a weak deformation band around 1410 cm^{-1}, and very intense absorptions of the out-of-plane deformation vibrations at 911 and 972 cm^{-1}. Other bands are absent in the region of the last two frequencies. The absorption at 1830 cm^{-1} corresponds to an ordinary overtone.

In the spectra of the isopropenylalkylacetylenes an intense absorption at 1616 cm^{-1} corresponds to the double bond. When a tertiary butyl radical is present in the 3 position, this frequency is shifted even more toward lower wavelengths. An absorption at 2235 cm^{-1}, somewhat higher than in the spectra of vinylalkylacetylenes, corresponds to the acetylenic bond. Another absorption, linked with the presence of the acetylenic grouping, is also found at a higher wavelength (1790 cm^{-1}).

---

*Enyne compounds. XXXI.

† Due to inaccurate calibration of the apparatus in the 2200-2300 cm^{-1} region, the values given earlier for the frequencies of the acetylenic grouping [6] in vinylacetylenes were somewhat high (by approximately 25 cm^{-1}). In the other portions of the spectrum the earlier-obtained and presently-found frequencies show satisfactory agreement.

TABLE 1

Compound	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR found	MR calculated	Found % C	Found % H	Calculated% C	Calculated% H	Yield (in %)
$C_5H_{11}-C\equiv C-CH=CH_2$	59.5—60° (20)	0.7782	1.4580	42.85	41.29	88.27, 88.27	11.71, 11.77	88.45	11.55	60
$C_6H_{13}-C\equiv C-CH=CH_2$	76—76.5 (20)	0.7873	1.4598	47.37	45.91	88.38, 88.30	11.60, 11.85	88.16	11.84	73
$C_8H_{17}-C\equiv C-CH=CH_2$	110.5—111 (20)	0.7964	1.4620	56.71	55.16	88.13, 88.13	11.97, 11.99	87.73	12.27	70
$CH_3-C\equiv C-C=CH_2$ $\quad\quad CH_3$	82—83 (760)	0.7518	1.4512	28.71	27.44	90.22, 90.18	10.21, 10.24	90.00	10.00	53
$C_2H_5-C\equiv C-C=CH_2$ $\quad\quad CH_3$	104.5—105.5 (760)	0.7572	1.4518	33.53	32.06	89.39, 89.31	10.69, 10.78	89.36	10.64	58
$CH_3-C\equiv C-C=CH_2$ $\quad\quad C(CH_3)_3$	59—60 (50)	0.7808	1.4538	42.37	41.29	88.79, 88.74	11.68, 11.61	88.53	11.48	67
$C_2H_5-C\equiv C-C=CH_2$ $\quad\quad C(CH_3)_2$	74—74.5 (50)	0.7774	1.4518	47.25	45.91	88.40, 88.31	11.70, 11.73	88.23	11.76	79
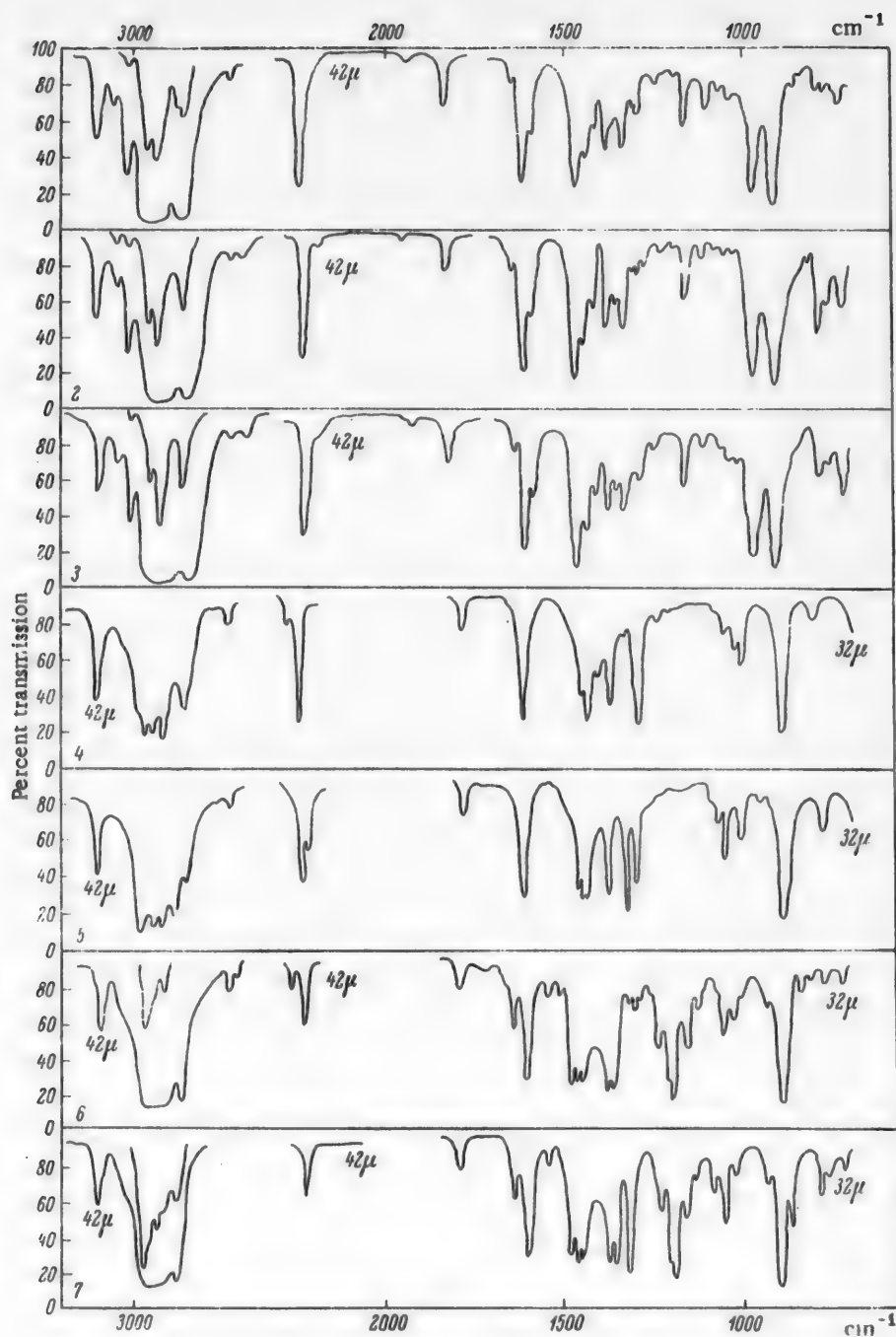
Infrared transmission spectra. 1) 1-Nonen-3-yne, 2) 1-decen-3-yne, 3) 1-dodecen-3-yne, 4) 2-methyl-1-penten-3-yne, 5) 2-methyl-1-hexene-3-yne, 6) 2-tert-butyl-1-penten-3-yne, 7) 2-tert-butyl-1-hexen-3-yne.

TABLE 2

Infrared Spectra of Hydrocarbons

	R—C≡C—CH=CH₂		R—C≡C—C=CH₂ CR'₃				
R	C₅H₁₁	C₆H₁₃	C₈H₁₇	R: CH₃	C₂H₅	CH₃	C₂H₅
				R': H	H	CH₃	CH₃
792 сл	786 ср	787 р	—	783 ср	777 сл	783 ср
—	—	—	807 сл	—	811 сл	—
839 сл	—	—	—	—	840 сл	872 ср
856 сл	—	—	892 о.с	892 о.с	892 о.с	892 о.с
911 о.с	911 о.с	910 о.с	—	—	—	—
—	—	—	—	955 сл	935 сл	935 сл
972 с	972 с	972 с	—	—	—	—
—	—	—	1008 ср	1008 ср	1003 сл	—
1034 сл	1025 сл	1015 сл	1026 сл	—	1025 ср	1025 сл
1064 сл	1047 сл	1037 сл	1055 сл	1053 ср	1054 ср	1051 ср
1097 ср	1073 сл	1067 сл	—	1077 сл	—	1086 ср
—	1110 сл	1112 сл	—	—	1126 сл	1135 сл
1162 ср	1162 ср	1163 ср	—	—	1161 сл	1161 ср
—	—	—	—	—	1194 с	1193 с
—	—	—	—	—	—	1205 с
1235 сл	1222 о.с	1249 сл	—	—	1240 ср	1234 сл
1289 сл	1273 сл	—	—	—	—	—
1299 сл	1292 ср	1290 сл	1293 с	—	1291 сл	—
—	1305 сл	—	—	—	1305 сл	—
1328 ср	1329 ср	1329 ср	1333 о.сл	1322 с	1320 сл	1321 с
1340 сл	1350 сл	1350 сл	—	—	—	—
1369 сл	—	—	—	—	1362 с	1360 с
1380 ср	1380 ср	1380 ср	1374 с	1374 с	1378 с	1381 с
1410 сл	1412 ср	1411 ср	1412 сл	—	—	—
1430 ср	1434 с	1432 с	1430 с	—	—	—
—	—	—	1442 с	1442 с	—	—
—	—	—	—	1452 с	1450 с	1452 с
1459 с	1462 о.с	1462 о.с	1462 с	1462 с	1464 с	1464 с
—	—	—	—	—	1481 с	1481 с
1586 ср	1589 ср	1587 ср	—	—	—	—
1608 с	1610 с	1609 с	1616 с	1616 с	1604 с	1603 с
1640 сл	1641 сл	1639 сл	—	—	1643 ср	1641 ср
—	—	—	1790 ср	1790 ср	1795 ср	1795 ср
1830 ср	1830 ср	1830 ср	—	—	—	—
1937 о.сл	1941 о.сл	1930 о.с	1938 о.сл	—	—	—
—	—	—	2046 о.сл	—	2052 сл	—
2183 сл	2184 сл	2187 сл	—	—	—	—
—	—	—	2215 ср	—	—	—
2229 с	2228 с	2226 с	2239 с	2235 с	2235 с	2221 с
—	—	—	2277 сл	—	2263 сл	—
2683 сл	2683 сл	2683 сл	—	—	—	—
2735 сл	2727 сл	2731 сл	2738 с	2729 сл	2741 сл	—
2862 с	2859 с	2856 с	2858 с	2849 с	—	—
2874 ?	—	—	—	2883 с	2871 с	2871 с
2934 о.с	2931 о.с	2925 о.с	2920 с	2921 с	2922 с	2917 с
2960 с	2955 с	2945 с	2955 с	2940 с	—	2943 с
—	—	—	2975 с	2978 с	2969 с	2972 с
3012 ср	3012 ср	3012 ср	—	—	—	—
3049 сл	3046 сл	3045 сл	—	—	—	—
3105 ср	3101 ср	3100 ср	3096 с	3096 с	3108 ср	3108 ср

Key: о. с very strong; с strong; ср medium; сл weak; о. слvery weak.

TABLE 3

Compound	ε_0	α	v_0	β	P_∞	μ (inD)
$CH_3{-}C{\equiv}C{-}C{=}CH_2$ $\quad\quad\quad\ \ \lvert$ $\quad\quad\quad\ CH_3$	2.2836	0.398	1.1368	0.186	37.68	0.65
$CH_3{-}C{\equiv}C{-}C{=}CH_2$ $\quad\quad\quad\ \ \lvert$ $\quad\quad\quad C(CH_3)_3$	2.2837	0.200	1.1368	0.152	51.73	0.67
$C_2H_5{-}C{\equiv}C{-}C{=}CH_2$ $\quad\quad\quad\quad\ \lvert$ $\quad\quad\quad\ \ C(CH_3)_3$	2.2836	0.140	1.1368	0.146	55.90	0.64

A very intense band at 892 cm^{-1} corresponds to the terminal methylene group. The valence vibrations of this group also give an absorption at high frequency (around 3100 cm^{-1}). The absorptions of the in-plane deformation vibrations (around 1410 cm^{-1}) are apparently masked by other bands.

The presence of a tert-butylgroup in the 3 position causes the appearance in the spectra of intense absorptions in the 1200-1250 cm^{-1} region due to the C-C vibrations (1194, 1205 cm^{-1}), and of intense absorption at 1480 cm^{-1} due to the CH deformation vibrations.

As a result, a study of some structurally new vinylacetylenic hydrocarbons confirmed the earlier established rules regarding the effect exerted by substituents in different positions of the vinylacetylene system on the infrared pattern.

EXPERIMENTAL

The method of alkylating vinylacetylene was described earlier [1]. Isopropenylacetylene and tert-butylvinylacetylene were obtained from the corresponding alcohols [7, 8]. They were alkylated in the same manner as the vinylacetylenes. The yields and analytical data for the synthesized compounds are given in Table 1. The experimental data on measuring the dipole moments are given in Table 3. The same as in the previous paper, the dipole moments were determined by measuring the dielectric permeability of dilute solutions using the pulsation method [5].

The infrared spectra of the investigated hydrocarbons are given in Table 2 (some of the very weak absorptions are omitted). An IKS-14 spectrophotometer was used to take the spectra, using a NaCl prism up to 1830 cm^{-1}, and then a LiF prism. The layer thickness was usually 0.035 mm.

SUMMARY

1. The alkylation of vinylacetylene, isopropenylacetylene, and tert-butylvinylacetylene gave a series of vinylacetylenic hydrocarbons.

2. The infrared spectra of the synthesized vinylacetylenic hydrocarbons were investigated, and here the earlier established rules were confirmed.

3. The dipole moments of three hydrocarbons (2-methyl-1-penten-3-yne, 2-tert-butyl-1-penten-3-yne, and 2-tert-butyl-1-hexen-3-yne) were measured.

LITERATURE CITED

[1] R. A. Jacobson and W. H. Carothers, J. Am. Chem. Soc. 55, 1622 (1933).

[2] W. F. Anzilotti and R. R. Vogt, J. Am. Chem. Soc. 61, 573 (1939).

[3] C . D. Hurd and F. L. Cohen, J. Am. Chem. Soc. 53, 1073 (1931).

[4] Zh. I. Iotsich, J. Russ. Chem. Soc. 39, 654 (1907).

[5] A. A. Petrov, K. S. Mingaleva and B. S. Kupin, Proc. Acad. Sci. USSR 123, 298 (1958).*

[6] A. A. Petrov, Yu. I. Porfir'eva, and G. I. Semenov, J. Gen. Chem. 27, 1167 (1957).*

[7] I. A. Favorskaya, J. Gen. Chem. 18, 53 (1948).

[8] K. A. Ogloblin, J. Gen. Chem. 18, 2153 (1948).

*Original Russian pagination. See C. B. Translation.

INVESTIGATIONS ON CONJUGATED SYSTEMS *

CIX. THE DIRECTION OF HYDRATION OF ISOPROPENYLALKYL-ACETYLENES

B.S. Kupin and A.A. Petrov

Leningrad Lensovet Institute of Technology

Vinylalkylacetylenes add on water under the conditions of the Kucherov reaction [1] and over heterogeneous catalysts [2] with formation of propenylalkyl ketones with a small amount of vinyl alkyl ketones. The sequence of addition of water is here not the same as the sequence of addition of hydrogen halides [3]. We attributed this difference to the special features of the mechanism of addition of water and hydrogen halides (nucleophilic attack in one case and electrophilic attack in the other) and to the facility of redistribution of the electron density in molecules of vinylalkylacetylenes [1].

Alkyl- and alkenylacetylenes of all possible types add on water only with formation of the corresponding methyl ketones [4, 5]. Unsymmetrical dialkylacetylenes form isomeric ketones in nearly the same quantities [6,7].

To complete the investigation of the relation between structure of vinylacetylenic hydrocarbons and sequence of addition of water, it was necessary to study the hydration of isopropenylalkylacetylenes. These hydrocarbons on the one hand contain the structure of vinylalkylacetylenes, which gave grounds for expecting addition of hydroxyl to the first acetylenic carbon, and on the other hand they include the structure of isopropenylacetylene which adds on water with formation of methylisopropenyl ketone.

Another reason for the importance of this work is that isopropenylalkyl-acetylenes contain a fragment of the molecule of vinylisopropenylacetylene for which I.N. Nazarov had established a fully specific and unexpected sequence of addition of water (the hydroxyl enters closer to the substituted vinyl group) [8]. The causes of this orientation of water in this industrially important reaction have not previously been clarified.

We ran experiments on hydration of two representatives of the isopropenylalkylacetylene series — 2 methyl-1-penten-3-yne and 2-methyl-1-hexen-3-yne. In this case we should expect formation of three unsaturated ketones depending on the sequence of addition of water.

$$R-CH_2-CO-C=CH_2 \longrightarrow R-CH_2-CO-CH(CH_3)_2$$
$$(I) \quad | \quad CH_3$$

$$R-C\equiv C-C=CH_2 \longrightarrow R-CO-CH_2-C=CH_2 \quad | \quad CH_3$$
$$| \quad CH_3 \qquad\qquad | \quad CH_3 \qquad\qquad R-CO-CH_2-CH(CH_3)_2$$

$$\longrightarrow R-CO-CH=C-CH_3$$
$$| \quad CH_3$$
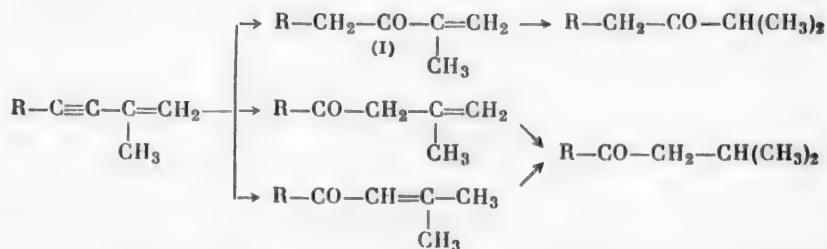
For R = CH_3 (addition to isopropenylmethylacetylene) all of these ketones have been described in the literature [9, 10].

In actuality, isopropenylalkyl ketones were predominantly formed; their structure was confirmed by comparison of their constants with those of authentic specimens, by hydrogenation to saturated ketones, and by the ultraviolet and infrared spectra.
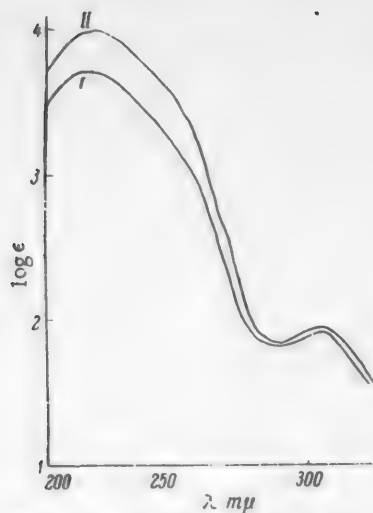
---

* Enynic compounds. XXXII.

Fig. 1. Ultraviolet spectra of hydration products. I) Isopropenylacetylene (ethylisopropenyl ketone); II) isopropenylethylacetylene (propylisopropenyl ketone).

Fig. 2. Infrared transmission spectra. 1) 2)Methyl-1-penten-3-yne, 2) product of its hydration (ethylisopropenyl ketone), 3) product of hydrogenation of the latter (ethylisopropyl ketone), 4) authentic ethylisopropyl ketone, 5) authentic methylisobutyl ketone, 6) product of hydration of propenylethylacetylene (propylpropenyl ketone).

The ketone prepared from isopropenylmethylacetylene has a boiling point and refractive index quite different from those of both of the forms of mesityl oxide and very similar to the literature constants cited for isopropenylethyl ketone.

Its ultraviolet spectrum contained maxima characteristic only of the conjugated C=C-C=O grouping (220 and 305 mμ); the maximum of the unconjugated carbonyl was absent (280 mμ) (Fig. 1).

The infrared spectrum of this ketone also contained the strong frequencies of a conjugated double bond (1620 cm^{-1}) and of the carbonyl group (1664 cm^{-1}), as well as the frequency of the CH$_2$=C- group (936 cm^{-1})
      |
     CH$_3$
[11] (Fig. 2, curve 2).

Hydrogenation over Pd/CaCO$_3$ converted the unsaturated ketone into ethylisopropyl ketone,which has been described in the literature. Examination of the infrared spectrum of the latter showed it to contain a small admixture (about 9% of methylisobutyl ketone* (Fig. 2, curves 3-5).

Consequently all of the formulas, except (I), for the main product of hydration of methylisopropenylacetylene are excluded.

Similar results were obtained in the investigation of propylisopropenyl ketone – the product of hydration of isopropenylethylacetylene.

The order of addition of water to vinylmethylacetylene is opposite to that of the addition to isopropenylmethylacetylene. This difference is of outstanding theoretical interest. If we start from the hypothesis that the sequence of addition is determined by the relative polarity of each of the acetylenic atoms of the hydrocarbon and if we

*Judging by the ratio of intensities of the bands characteristic of ethylisopropyl ketone (981, 1026,and 1103 cm^{-1}) and of methylisobutyl ketone (1176 cm^{-1}), the infrared spectrum of the investigated specimen of ethylisopropyl ketone most closely resembles the spectrum of a mixture of the authentic ketones containing about 9% of methylisobutyl ketone. Ethylisopropyl ketone was prepared by the oxidation of ethylisopropylcarbinol (in turn prepared from isobutyraldehyde and ethylmagnesium bromide). The methylisobutyl ketone was a commercial product.
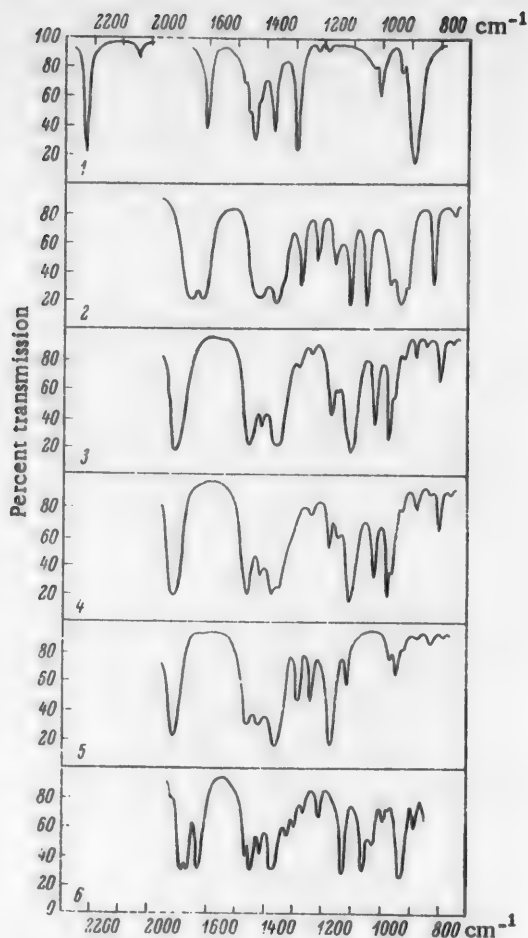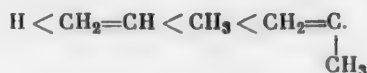
take account of I.N. Nazarov's data for the hydration of dienynes, then we obtain the following order of increasing electronegativity of radicals:

$$H < CH_2=CH < CH_3 < CH_2=\underset{\underset{CH_3}{|}}{C}.$$

These data do not afford an explanation of the characteristic addition of water to vinylalkylacetylenes by shift of the electron density in their molecules under the influence of radicals, since in the case of isopropenylalkylacetylenes both of the alkyls intensify the shift in the same direction, and the sequence of addition is reversed (relative to vinylalkylacetylenes).
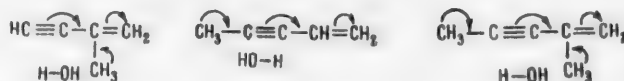
Elucidation of the causes of the observed regularity calls for further investigations.

EXPERIMENTAL

<u>Hydration of isopropenylmethylacetylene.</u> The hydrocarbon was prepared by dehydration of dimethylpropynylcarbinol * by distillation with 5% sulfuric acid. Yield about 60%.

B.p. 82-83°, d_4^{20} 0.7502, n_D^{20} 1.4480.

Infrared spectrum (principal frequencies): 891 (very strong), 937 (weak), 1009 (medium), 1026 (weak) 1188 (weak), 1221 (weak), 1294 (strong), 1372 (strong), 1413 (medium), 1434 (strong), 1443 (strong) 1462 (medium), 1611 (strong), 1790 (medium), 2043 (weak), 2223 (strong), 2728 (weak), 2852 (strong), 2913 (very strong), 2943 (strong), 2963 (very strong), 3092 (medium), cm^{-1} (Fig. 2, curve 1).

10 g of the hydrocarbon was intensively stirred with a solution of 3.1 g HgO in 200 ml of 12% sulfuric acid and 10 g of ferric sulfate for 8 hours. The liquid was distilled with steam and the upper layer was separated. The ketone was extracted from the lower layer with ethyl chloride. A total of about 4.5 g of ethylisopropenyl ketone was obtained (yield 47.5% on the hydrocarbon).

B.p. 118-121° d_4^{20} 0.8512, n_D^{20} 1.4312.

Found%: C 73.75, 73.63; H 10.17, 10.27. $C_6H_{10}O$. Calculated %: C 73.47; H 10.20 Infrared spectrum: 820 (strong), 913 (medium), 933 (very strong), 946 (strong), 973 (medium), 1047 (strong), 1106 (strong), 1160 (strong), 1221 (strong), 1281 (strong), 1360 (very strong), 1373 (strong), 1422 (strong), 1448 (very strong), 1460 (strong), 1623 (very strong), 1674 (very strong), 1688 (strong) cm^{-1} (Fig 1, curve 2).

2,4-Dinitrophenylhydrazone: m.p. 141-142° (from alcohol).

Found %: N 20.56, 20.01. $C_{12}H_{14}O_4N_4$. Calculated %: N 20.14.

Semicarbazone: m.p. 155-156° (from alcohol).

The following constants for ethylisopropenyl ketone are reported in the literature: b.p. 119° $d_4^{23.5}$ 0.850, $n_D^{23.5}$ 1.4270 [9]. The following constants are reported for the two forms of mesityl oxide: CH_3-CO-CH_2-C=CH_2-CH_3 b.p. 121.4°, d_4^{20} 0.84111, n_D^{20} 1.42130; 2,4-dinitrophenylhydrazone, m.p. 70°; CH_3-CO-CH=$\underset{\underset{CH_3}{|}}{C}$-$CH_3$: b.p. 130° d_4^{20} 0.858, n_D^{20} 1.444; 2,4-dinitrophenylhydrazone: m.p. 203° [10].

Reduction of 1.7 g ketone in 10 ml methyl alcohol in presence of 3 g of Pd/CaCO$_3$ was accompanied by adsorption of 415 ml H$_2$ (749.8 mm, 19°) or 96.6% of the theoretical. The reaction mixture was decanted from

* Dimethylpropynylcarbinol was prepared by the action of acetone on methylacetylenemagnesium bromide. For one of the hydration experiments isopropenylmethylacetylene was prepared by the action of ethyl bromide on the sodium derivate of isopropenylacetylene in liquid ammonia. When using the latter method the possibility of isomerization of 2-methyl-1-buten-3-yne to 4-methyl-3-buten-1-yne (under the influence of excess of sodium amide) must be taken into consideration.

the catalyst diluted with ether and washed with saturated $CaCl_2$ solution. The ether was driven off to leave 0.6 g of ethylisopropyl ketone.

B.p. 113-114°, d_4^{20} 0.8078, n_D^{20} 1.3970.

Infrared spectrum: 761 (very weak), 802 (medium), 844 (very weak), 881 (weak), 929 (weak), 981 (strong), 1026 (strong, 1103 (very strong), 1179 (medium), 1292 (weak), 1368 (very strong), 1415 (strong), 1464 (very strong), 1712 (very strong) cm^{-1}.

2,4-Dinitrophenylhydrazone: m.p. 109-110° (from alcohol)[12].

Found %: N 20.08, 19.95. $C_{12}H_{16}O_4N_4$. Calculated %: N 20.00

The same dinitrophenylhydrazone was obtained from the liquid distilled off from the aqueous alcoholic solution. Methylisobutyl ketone 2,4-dinitrophenylhydrazone melts at 95° [13].

Hydration of isopropenylethylacetylene. 3.2 g HgO in 190 ml of 14% sulfuric acid was placed in a three-necked flask with a reflux condenser. The hydrating mixture was heated to 70° and dropwise addition was made (vigorous stirring) of 11 g of the hydrocarbon in the course of 0.5 hour. After the addition, stirring was continued for another 4 hours at the same temperature. The mixture was then worked up as in the preceding experiment to give 3.5 g (yield 49.4% on the reacted hydrocarbon).

B.p. 140-141°, 80-81° (100 mm), d_4^{20} 0.8500, n_D^{20} 1.4376.

Found %: C 75.30, 75.40; H 10.78, 10.73. $C_7H_{12}O$. Calculated %: C 75.00; H 10.71.

Infrared spectrum: 761 (weak), 844 (weak), 885 (medium), 891 (weak), 930 (very strong), 989 (weak), 1025 (medium), 1060 (strong), 1123 (very strong), 1209 (medium), 1261 (weak), 1295 (medium), 1324 (medium), 1371 (very strong), 1411 (strong), 1451 (very strong), 1463 (strong), 1625 (very strong), 1674 (very strong), 1687 (strong) cm^{-1} (Fig. 1, curve 6).

Hydrogenation of 0.45 g of the ketone in 5 ml of methyl alcohol in presence of 1 g Pd/$CaCO_3$ (101 ml H_2 was absorbed at 754 mm and 21°, or 96% of the theoretical quantity) gave a saturated ketone.

2,4-Dinitrophenylhydrazone: m.p. 85°.

Semicarbazone: m.p. 118-119° [13], in agreement with the literature value for propylisopropyl ketone.

The corresponding derivatives of ethylisobutyl ketone melt at 75 and 152° [14].

SUMMARY

1. The sequence of addition of water to 2-methyl-1-penten-3-yne and 2-methyl-1-hexen-3-yne was investigated.

2. It was established that in both cases isopropenylalkyl ketones are formed, i.e., the introduction of a methyl group in the 3 position of vinylalkylacetylene reverses the sequence of addition of water.

3. Hydrogenation of these ketones over palladium gave the corresponding alkylisopropyl ketones.

LITERATURE CITED

[1] A.A. Petrov and B.S. Kupin, Zhur. Obshchei Khim. 28, 1999 (1958); 29, 2281 (1959).*

[2] Yu.A. Gorin and L.P. Bogdanova, Zhur. Obshchei Khim. 28, 1144 (1958).*

[3] E.A. Leporskaya and A.A. Petrov, Zhur. Obshchei Khim. 23, 1471 (1953).*

[4] R.J. Thomas, K.N. Campbell, G.F. Hennion. J. Am. Chem. Soc. 60, 719 (1938).

[5] K.A. Ogloblin, Zhur. Obshchei Khim 18, 2153 (1948); I.A. Favorskaya, Zhur. Obshchei Khim. 19, 2051 (1949).*

[6] E. Mowat, J. Smith, J. Chem. Soc. 19 (1938).

[7] A. Michael, Ber. 38, 2143 (1906).

*Original Russian pagination. See C. B. Translation.

[8] I. N. Nazarov, Uspekhi Khim. 20, 71 (1951).

[9] J. Colonge, Bull. Soc. Chim.(5), 3, 2116 (1936).

[10] F. H. Stross, C. M. Gable, G.C. Raunds, J. Am. Chem. Soc. 69, 1627, 1630 (1947).

[11] W.H.T. Davison, G.R. Bates, J. Chem. Soc. 2607 (1953).

[12] H.Burton, Ch.W. Shoppce, Ch.L. Wilson, J. Chem. Soc., 720 (1933).

[13] I.N. Nazarov and A.I. Kakhniashvili, Zhur. Obschchei Khim., Sbornik II, 896 (1954).

[14] Slovar' org. soed. (Dictionary of Organic Compounds) (1949).

SOME 8-SUBSTITUTED DERIVATIVES OF CAFFEINE

R.G. Glushkov, E.S. Golovchinskaya
and O.Yu. Magidson

S. Ordzhonikidze All-Union Scientific Research
Institute of Chemical Pharmaceutics

The valuable pharmacological properties of tetrazoles, one representative of which is the extensively employed Metrazole (α,β-pentamethylenetetrazole) [1], prompted us to synthesize tetrazolo (1,5−8',9') caffeine (I). It seemed probable that the association of the tetrazole ring with such a powerful cardiovascular agent as caffeine should lead to compounds with high activity. The first step in the synthesis was the conversion of 8-chlorocaffeine by treatment with hydrazine hydrate into 8-hydrazinocaffeine [2]. Reaction of the latter with nitrous acid gave (I). Heating of 8-hydrazinocaffeine with formamide also led to a high yield of 1,2,4-triazolo (4,5−8',9')-caffeine (II). On the other hand, attempts to close the triazole ring by the action of boiling 85% HCOOH on 8-hydrazinocaffeine were unsuccessful.
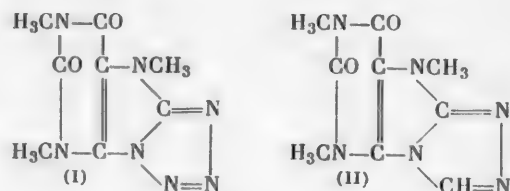
The physical and chemical properties of these substances − the negative reaction for the hydrazine group, insolubility in acids, and the explosive properties of tetrazolo (1,5−8',9') caffeine − confirm that they contain a third ring condensed with the imidazole portion of the caffeine molecule.

From 8-chloromethylcaffeine [3] have also been synthesized derivatives of 8-aminomethylcaffeine [4] substituted in the amino group by a bis-β-chloroethyl residue. It was synthesized by condensation of 8-chloromethylcaffeine with diethanolamine followed by treatment of the 8-(bis-β-hydroxyethyl) aminomethylcaffeine with thionyl chloride.

EXPERIMENTAL

Tetrazolo (1,5−8',9') caffeine (I). To a suspension (cooled to−5°) of 5 g 8-hydrazinocaffeine in 40 ml 10% sulfuric acid was added dropwise, in the course of 20 minutes, a solution of 3.5 g sodium nitrite in 7 ml water (towards the end of the addition a sample of the reaction mass turned starch−iodide paper blue). 4.85 g of product was isolated and chloroform extraction of the mother liquor gave another 0.15 g. The compound was crystallized three times from 96% alcohol; decomp. p. approx. 250°; explosion at about 180° on rapid heating. Tetrazolo (1,5−8',9') caffeine forms fine, colorless needles. It turns red on standing in the light; it is readily soluble in chloroform in the cold, in alcohol, and benzene on heating, sparingly soluble in ether and water. Unlike 8-hydrazinocaffeine, it does not reduce ammoniacal silver oxide.

Found %: C 41.07; H 4.22; N 41.63. $C_8H_9O_2N_7$. Calculated %: C 40.85; H 3.84; N 41.7.

1,2,4-Triazolo (4,5 8',9') caffeine (II). 4 g of 8-hydrazinocaffeine was stirred at the boil for 2 hours with

40 ml formamide. The cooled reaction mass deposited a precipitate which was suction-filtered and washed first with water and then with alcohol. Yield 3.7 g (88.52%) of 1,2,4-triazolo (4,5- 8',9') caffeine; fine needles with m.p. 233-234.5°. For analysis it was crystallized from 96% alcohol (1:100). Sparingly soluble in water and alcohol, insoluble in the majority of organic solvents; does not reduce ammoniacal silver oxide.

Found %: N 35.71. $C_9H_{10}O_2N_6$. Calculated %: N 35.89.

8-(Bis-β-hydroxyethyl)aminomethylcaffeine. 20 g 8-chloromethylcaffeine and 30 g diethanolamine were stirred 30 minutes at 100° to form a yellowish solution which later changed to a viscous mass. This was cooled and dissolved in 60 ml chloroform; the solution was washed twice with water (each time with 10 ml) and dried with calcined sodium sulfate. The chloroform was driven off to leave 17 g of substance with m.p. 143-147°. Extraction of the wash liquors with chloroform yielded a further 5 g with m.p. 140-146°. The unpurified product (22 g) was crystallized from 250 ml of carbon-containing methylethyl ketone to give 21 g (82%) of small spheres of 8-(bis-β-hydroxyethyl)-aminomethylcaffeine with m.p. 148-150°; the product was amorphous; the pH of the 5-10% aqueous solution was approx. 7.5; readily soluble in water, chloroform,and alcohol, difficultly soluble in ether, benzene,and ethyl acetate.

Found %: N 22.55. $C_{13}H_{21}O_4N_5$. Calculated %: N 22.55.

8-(Bis-β-hydroxyethyl) aminomethylcaffeine hydrochloride. Prepared by treatment of a solution of the base in anhydrous alcohol with alcoholic hydrogen chloride. Crystallizes from anhydrous alcohol as plates with m.p. 199-201°.

Found %: Cl 9.55. $C_{13}H_{22}O_4N_5Cl$. Calculated %: Cl 10.21

8-(Bis-β-chloroethyl) aminomethylcaffeine. To a solution of 10 g of 8-(bis-β-hydroxyethyl)aminomethyl-caffeine in 80 ml of dry chloroform was gradually added at 20° a solution of 50 ml of $SOCl_2$ in 50 ml chloroform. A yellow precipitate came down. The reaction mass was boiled 3.5 hours (it formed a transparent solution). The chloroform and excess of thionyl chloride were driven off and the residue (of dark resin) was treated with 100 ml of ice water; the solution was then filtered and neutralized with saturated sodium carbonate solution; the resulting precipitate was crystallized from 70 ml of 96% alcohol (in presence of carbon); yield of 8-(bis-β-chloroethyl) aminomethylcaffeine 7.4 g (66%), m.p. 136.5-137.5°. Sparingly soluble in ether and water, readily soluble in chloroform, alcohol, acetone, benzene,and dilute acids.

Found %: Cl 20.06, 20.47. $C_{13}H_{19}O_2N_5Cl_2$. Calculated %: Cl 20.40.

SUMMARY

1. Reaction of 8-hydrazinocaffeine with nitrous acid or formamide results in cyclization with formation of tetrazolo (1,5- 8',9') caffeine in the former case and of 1,2,4-triazolo (4,5- 8',9') caffeine in the latter case.

2. 8-(Bis-β-chloroethyl) aminomethylcaffeine was synthesized from 8-chloromethylcaffeine.

LITERATURE CITED

[1] R.G. Glushkov and E.S. Golovchinskaya,*Synthesis of α,β-cyclopentamethylenetetrazole", Zhur. Priklad. Khim. 24, 920 (1959).*

[2] L. Cramer, Chem. Ber. 27, 3090 (1894).

[3] German Patent 146714; Frdlz. 7, 670; E.S. Golovchinskaya, Zhur. Obshchei Khim. 18, 2129 (1948).

[4] E.S. Golovchinskaya and E.S. Chaman, Zhur. Obshchei Khim. 22, 535 (1952).*

*Original Russian pagination. See C. B. Translation.

# HERBICIDES AND PLANT GROWTH REGULATORS

XXXIV. A NEW METHOD OF PREPARATION OF
ARYLOXY-γ-BUTYRIC ACIDS

N. N. Mel'nikov and S.S. Kukalenko

Scientific Institute for Fertilizers and Insectofungicides

2,4-Dichlorophenoxy-γ-butyric and 2-methyl-4-chlorophenoxy-γ-butyric acids have recently been employed to some extent as agents for combating dicotyledonous weeds in leguminous crops [1, 2]. These agents are relatively innocuous to legumes and destroy many other dicotyledonous growths. This selectivity is due to the different rate of conversion of the compounds in different plants into 2,4-D. The aryloxy-γ-butyric acids are therefore of great practical interest and merit the closest attention. Only one metod of preparation of these compounds has been described in the literature — via aryloxy-γ-chloropropane and the nitrile [3]. But this method has many steps and necessitates use of the relatively expensive chlorobutyronitrile or of aryloxy-γ-chloropropane, both of which are difficult to prepare.

For preparation of aryloxy-γ-butyric acids, we made use of the reaction of phenates with butyrolactone which was recently applied successfully [4] to the synthesis of 3-indolyl-γ-butyric acid. Our experiments established that butyrolactone reacts with facility with alkali metal phenates and ammonium phenate at 80-200° with formation of the corresponding salts of aryloxy-γ-butyric acids in satisfactory yields. This reaction can be represented by the following general equation.

$$ArOMe + CH_2-CH_2CH_2CO \longrightarrow ArOCH_2CH_2CH_2COOMe.$$
$$\underset{O}{|\rule{2cm}{0pt}|}$$
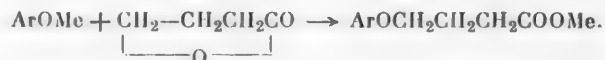
In this reaction with butyrolactone we tested not only unsubstituted but also substituted phenols as well as naphthol. The prepared compounds are listed with their properties in the table.

EXPERIMENTAL

We carried out the reaction of butyrolactone with phenates with use of a slight excess of butyrolactone. Two variants were employed.

First variant. To butyrolactone (heated to 120-140°) was gradually added with good stirring the finely pulverized phenate; the reaction mixture was held at this temperature for 20-40 minutes, cooled and dissolved in water; the aqueous solution was acidified with sulfuric acid. The organic acid and the phenol were extracted with ether; the acid was removed from the ether solution by shaking with aqueous sodium carbonate solution. The soda solution was acidified with sulfuric acid; the aryloxy-γ-butyric acid was filtered off and purified by recrystallization.

Second variant. An equimolar mixture of phenate and butyrolactone (10% excess) was refluxed in a flask with good stirring for several hours at 190-208°; the product was then isolated and purified as described above.

The compounds prepared and their properties are listed in the table. Some of the compounds have not previously been described.

TABLE

Properties of Aryloxy-γ-butyric Acids $ArOCH_2CH_2COOH$

Ar	Reaction temp.	Yield (in %)	Melting point		Analysis of acid by titration with KOH	
			found	literature	M found	M calc.
C_6H_5	130—200°	75	60—61°	60[5]	—	—
2-$CH_3C_6H_4$	130	70	76—77	—	198	194.1
					204	
4-FC_6H_4	130	71	107	106—107[6]	196	198.1
					193	
2,4-$Cl_2C_6H_3$	205—208	64	116—117	117—118[3]	—	—
1-$C_{10}H_7$	130	44	112—113	—	227	230.1
					233	

SUMMARY

A simple and convenient method was developed for the preparation of aryloxy-γ-butyric acids by reaction of butyrolactone with phenates of various phenols at elevated temperature. Some of the synthesized compounds have not previously been described.

LITERATURE CITED

[1] Nauka i peredovoi opyt v sel'skom khozyaistve, No. 9, 73 (1957).

[2] Proc. of the Ninth N.Z, Weed Control Confer. (Wellington, 1956).

[3] P. Synerholm and K. Zimmerman, Contr. Boyce Thompson Inst. 14, 369 (1947).

[4] F. N. Stepanov, Auth. Certif. No. 66,681.

[5] J. Bentley, H. Haworth, and Perkin, J. Chem. Soc. 69, 168 (1896).

[6] N.N. Mel'nikov and S.S. Kukalenko, Zhur. Obshchei Khim. 29, 3708 (1959).*

Received August 6, 1958

* Original Russian pagination. See C. B. Translation.

CHLOROMETHYLATION OF ETHERS OF DIHYDRIC
PHENOLS AND SOME OF THEIR TRANSFORMATIONS

N. N. Mel'nikov and M. V. Prilutskaya

The great lability of the chlorine in the molecule of benzyl chlorine and its derivatives, containing various functional groups in the benzene ring, make this group of compounds of considerable interest for the synthesis of many classes of compounds which can be obtained by replacement of the halogen by other groupings. Particularly interesting are benzyl chlorides containing alkoxy radicals in the aromatic ring, since they can be used for the synthesis of a series of physiologically active substances. The simplest method of preparation of alkoxybenzyl chlorides is chloromethylation. This method has been fairly extensively used for the synthesis of various substituted benzyl chlorides [1].

In continuation of our earlier work [2-4], we have now studied the chloromethylation of some ethers of pyrocatechol and hydroquinone. Since the literature has described the preparation of only o-dimethoxy- and p-dimethoxybenzyl chlorides [5-12], it was of interest to study the chloromethylation of ethers of higher molecular weight, especially since the literature indicates the impossibility of preparation of the corresponding derivatives of ethers of hydroquinone of higher molecular weight [8].

In the preceding communication we showed that the main products of chloromethylation of ethers of hydroquinone in acetic acid solution are 1,4-bis (chloromethyl)-2,5-dialkoxybenzenes [3], but that the corresponding dialkoxybenzyl chlorides could not be isolated in any appreciable quantity under these conditions. We therefore studied the chloromethylation in an aqueous medium with a deficiency of formaldehyde. These experiments showed that also in an aqueous medium the reaction goes with predominant formation of 1,4-bis-(chloromethyl)-2,5-di-alkoxybenzenes, and that only by using a deficiency of formaldehyde can dialkoxybenzyl chloride be obtained together with a certain quantity of the bischloromethyl derivative.

It is interesting to note that the main products of the chloromethylation of ethers of pyrocatechol are 3,4-dialkoxybenzyl chlorides in yields of 60-75%.

The compounds that we prepared and their properties are listed in Table 1. Their structure was confirmed by oxidation to the corresponding dialkoxybenzoic acids which have been described in the literature [13-15].

Bis-(chloromethyl)-dialkoxybenzenes are prepared with great difficulty and in very low yields from ethers of pyrocatechol. This is presumably due to the poor stability of 3,4-dialkoxybenzyl chlorides, which enter, under very mild conditions, into condensation with the liberated hydrogen chloride, to form 2,3,6,7-tetraalkoxy-9,10-dihydroanthracenes. This reaction has been closely studied for the case of condensation of 3,4-dimethoxybenzyl chloride [5,6,16,17]. It must be pointed out, however, that the susceptibility to condensation with formation of 2,3,6,7-tetraalkoxy-9,10-dihydroanthracenes decreases with increasing size of the ether radical.

Reaction of our synthesized dialkoxybenzyl chlorides with tertiary amines gave salts of quaternary ammonium bases not previously described in the literature. Reaction with salts of thiocyanic acid and cyanides gave the corresponding thiocyanates and nitriles of arylacetic acids, also not described in the literature. Saponification of the nitriles gave previously undescribed arylacetic acids. The compounds that we synthesized are presented with their properties in Table 2.

Reaction of 1,4-bis-(chloromethyl)-2,5-dialkoxybenzenes with alcohol in presence of potassium hydroxide gave previously undescribed bis-(ethoxymethyl)-dialkoxybenzenes. Their properties are given in Table 2.

TABLE 1

Properties of Products of Chloromethylation of Ethers of Pyrocatechol and Hydroquinone

Name	Melting point	Yield (in %)	% Cl found	calc.
3,4-Dimethoxybenzyl chloride	50—51°*	63	19.30, 19.25	19.03
3,4-Diethoxybenzyl chloride	126—127	66	16.08, 16.25	16.55
3,4-Dipropoxybenzyl chloride	99—101	64.5	14.28, 14.56	14.63
3,4-Dibutoxybenzyl chloride	86—87	74	12.78, 12.91	13.12
1,4-Bis(chloromethyl)-2,5-dimethoxybenzene	161**	45	29.92, 29.99	30.17
2,5-Diethoxybenzyl chloride***	—	64	16.49, 16.55	16.55
1,4-Bis(chloromethyl)-2,5-diethoxybenzene	150—151	42	26.82, 27.00	26.96
1,4-Bis(chloromethyl)-2,5-dipropoxybenzene	83—84	50	24.34, 24.40	24.36
1,4-Bis(chloromethyl)-2,5-dibutoxybenzene	81—82	55	22.14, 22.30	22.23

* According to the literature [5]: m.p. 51°.

** According to the literature [8, 9]: m.p. 161°.

*** B.p. 112° (1 mm) d_4^{20} 1.1150, n_D^{18} 1.5271.

EXPERIMENTAL

Chloromethylation of ethers of pyrocatechol. A mixture of 0.1 mole pyrocatechol ether, 10 g paraformaldehydr, 3-3.5 g phosphoric acid, 15-20 g metallic mercury, 200 ml glacial acetic acid, and 40 ml concentrated hydrochloric acid was well stirred and saturated with hydrogen chloride at 30-45° (the temperature depending on the ether used) for 2.5 hours. After cooling, the reaction mixture was poured into 1 liter of iced water and the precipitate was filtered off and washed with a small quantity of acetic acid and with water until neutral. The product was recrystallized from acetone. Properties of the compounds are given in Table 1.

Recrystallization of 3,4-dimethoxybenzyl chloride and of 3,4-diethoxybenzyl chloride from toluene led to nearly quantitative formation of the corresponding 2,3,6,7-tetraalkoxy-9,10-dihydroanthracenes. 3 g of 3,4-dimethoxybenzyl chloride thus gave 2.4 g of 2,3,6,7-tetramethoxy-9,10-dihydroanthracene with m.p. 230-232°; the literature [10] reports m.p. 235°.

Found %: C 72.20, 72.32; H 7.00, 6.82. $C_{18}H_{20}O_4$. Calculated %: C 72.00; H 6.66.

3 g of 3,4-diethoxybenzyl chloride gave more than 2 g of previously undescribed tetraethoxydihydroanthracene with m.p. 270-271°.

Found %: C 74.68, 74.52; H 7.50, 7.82. M 350, 354. $C_{22}H_{28}O_4$. Calculated %: C 74.17; H 7.85; M 356.

Oxidation of 2,3,6,7-tetraethyoxy-9,10-dihydroanthracene with permanganate in an alkaline medium gave 3,4-diethoxybenzoic acid with m.p. 165-166°.

Oxidation of 3,4-dialkoxybenzyl chlorides. We oxidized the products of chloromethylation of ethers of pyrocatechol with alkaline permanganate with the aim of establishing their structure. A mixture of 0.015 mole of dialkoxybenzyl chloride with 200 ml of 1% aqueous sodium hydroxide solution was heated to 60° and addition was made at this temperature of a solution of 2 g of potassium permanganate in 200 ml water. The reaction mixture was then boiled for 30 minutes. The next day the manganese dioxide was filtered off and the acids were isolated in the usual manner. After recrystallization the acids were analyzed by titration with alkali. From 3, 4-dimethoxy-, 3,4-diethoxy-, 3,4-dipropoxy-, and 3,4-dibutoxybenzyl chlorides were obtained acids with m.p. respectively of 178-180°, 165-166°, 155-157° and 141-142°. The constants are nearly identical with those given in the literature [13-15].

Chloromethylation of ethers of hydroquinone. A mixture of 0.1 mole hydroquinone ether, 0.23 mole formaldehydr, 1.5 g phosphoric acid, 5 g metallic mercury, and 150 ml concentrated hydrochloric acid was saturated with gaseous hydrogen chloride at 60-80° for 4 hours. After cooling, the precipitate was filtered off, washed with 50% acetic acid and with water, and recrystallized from acetone. The compounds obtained by this procedure are listed in Table 1 together with their properties.

For the purpose of preparation of 2,5-diethoxybenzyl chloride, we carried out the chloromethylation of hydroquinone diethyl ether under the following conditions: 0.1 mole of the diethyl ether, 1 g phosphoric acid, 5 g metallic mercury, 0.12 mole formaldehyde (37% solution), and 50 ml concentrated hydrochloric acid were saturated

with gaseous HCl at 60-65° for 4 hours. The reaction mixture was worked up in the appropriate manner to give 8.4 g of 1,4-bis-(chloromethyl)-2,5-diethoxybenzene and 13.8 g of 2,5-diethoxybenzyl chloride with b.p. 112° (1 mm), n_D^{18} 1.5270 d_4^{20} 1.1150.

Found %: 61.60, 61.41; H 7.02, 6.96; Cl 16.49, 16.55. $C_{11}H_{15}O_2Cl$. Calculated %: C 61.53; H 6.99; Cl 16.55.

Reaction of chloromethyl derivatives of ethers of hydroquinone with alcohol in presence of alkali. A solution of 0.01 mole chloromethyl derivative of hydroquinone ether in 30-40 ml 1 N KOH solution in alcohol was boiled one hour in a flask under a reflux condenser. After cooling, the reaction mixture was diluted with double the volume of water and the solid product was filtered and purified by recrystallization from aqueous alcohol. The liquid components were extracted with ether and washed with water; after drying and removal of the ether, they were distilled in vacuo. The compounds that we obtained and their properties are listed in Table 2.

Preparation of 3,4-dialkoxybenzyl thiocyanates. A study of the reaction of salts of thiocyanic acid with 3,4-dialkoxybenzyl chlorides established that 3,4-dimethoxy- and 3,4-diethoxybenzyl chlorides give a complex mixture of products from which the corresponding thiocyanates could not be isolated in any appreciable quantity. Thiocyanates of higher molecular weight were obtained by the following procedure: A mixture of 0.05 mole 3,4-dialkoxybenzyl chloride, 5.7 g ammonium thiocyanate, 2.9 sodium chloride,and one g phosphoric acid in 200 ml acetone was refluxed in a flask at 56-57° with good stirring for 2.5 hours. At the conclusion of the reaction, the greater part of the acetone was driven off; the residue was treated with cold water, and the crystalline product was filtered off and recrystallized from alcohol. The compounds that we obtained are listed in Table 2 together with their properties.

Preparation of 3,4-dialkoxyphenylacetonitriles. Just as in the case of salts of thiocyanic acid, the lower-molecular representatives of 3,4-dialkoxybenzyl chlorides react with salts of hydrocyanic acid to form resinous masses. Other compounds were prepared by the following procedure: A solution of 3.68 g sodium cyanide and 2.9 g sodium chloride in 12 ml water was added with good stirring to a mixture (heated to 40°) of 0.05 mole 3, 4-dialkoxybenzyl chloride, one g phosphoric acid, 10 g metallic mercury, and 250 ml acetone. The reaction mixture was thereupon refluxed for 2.5 hr. The greater part of the acetone was then distilled off on a water bath and the residue was poured into 500 ml cold water. After standing for 2 hr, the precipitate was filtered and re-crystallized from alcohol. The prepared compounds and their properties are set forth in Table 2.

Hydrolysis of 3,4-dialkoxyphenylacetonitriles. 3 g of nitrile was dissolved in 50 ml ether and 50 ml concentrated sulfuric acid. The solution was refluxed in a flask for 10 hr. After standing for 24 hr, the mass was heated for another 5 hr. At the conclusion of the reaction, the ether layer was separated, and the acid layer was diluted with double the volume of water and extracted with ether. The combined ether extracts were washed with water and dried and the ether was driven off. The acids were recrystallized from aqueous alcohol. The synthesized products are set forth in Table 2.

Preparation of salts of quaternary ammonium bases. To a solution of 0.01 mole of chloromethyl derivative in 20 ml methyl or ethyl alcohol was gradually added trimethyl- or triethylamine (in the case of trimethylamine the addition was made at -5° and in the case of triethylamine at room temperature). After being stirred for 30-40 min, the mixture was heated to 65-75°. The alcohol was then distilled off and the residue treated with 20-30 ml of dry ether. The crystalline precipitate of salt was filtered, washed with dry ether and recrystallized from alcohol. It is interesting to note that products of replacement of chlorine by ethoxyl were obtained in 2-5% yield as by-products of this reaction. The prepared compounds and their properties are set forth in Table 2.

SUMMARY

1. The chloromethylation of ethers of pyrocatechol and hydroquinone was studied. The main products of chloromethylation of pyrocatechol ethers are shown to be 3,4-dialkoxybenzyl chlorides, while those from hydroquinone ethers are 1,4-bis (chloromethyl)-2,5-dialkoxybenzenes. Chloromethylation of hydroquinone ethers with one mole of formaldehyde gives a mixture of 1,4-bis(chloromethyl)-2,5-dialkoxybenzene and 2,5-dialkoxybenzyl chloride.

2. Studies were made of the reactions of chloromethyl derivatives of pyrocatechol and hydroquinone ethers with tertiary amines, salts of hydrocyanic and thiocyanic acids, and alcohol in presence of potassium hydroxide. A series of previously undescribed compounds was synthesized. Their properties are set forth in Table 2.

TABLE 2

Properties of Derivatives of Dialkoxybenzenes

Formula	Melting point	Yield (in %)	% C found	% C calc.	% H found	% H calc.	M found	M calc.
$2,5\text{-}(CH_3O)_2C_6H_2(CH_2OC_2H_5)_2\text{-}1,4$	55°	90	66.00 / 65.96	66.14	8.58 / 8.48	8.66	—	—
$2,5\text{-}(C_2H_5O_2)_2C_6H_3CH_2OC_2H_5$*	B. p. 120—122° (2 mm)	94	69.30 / 69.50	69.64	9.20 / 8.78	8.92	—	—
$2,5\text{-}(C_2H_5O)_2C_6H_2(CH_2OC_2H_5)_2\text{-}1,4$	69—70	93	67.74 / 67.77	68.08	9.26 / 9.53	9.22	281 / 280	282
$2,5\text{-}(C_3H_7O)_2C_6H_2(CH_2OC_2H_5)_2\text{-}1,4$	36—37	89	69.25 / 69.40	69.67	9.55 / 9.82	9.67	308 / 309	310
$2,5\text{-}(C_4H_9O)_2C_6H_2(CH_2OC_2H_5)_2\text{-}1,4$**	B. p. 162—164° (5 mm)	85	71.08 / 71.22	71.00	10.16 / 10.09	10.00	—	—
$3,4\text{-}(C_3H_7O)_2C_6H_3CH_2SCN$	123—124	38	N5.23 / 5.18	5.28	S11.79 / 11.85	12.07	261 / 260	265
$3,4\text{-}(C_4H_9O)_2C_6H_3CH_2SCN$	72—73	70	N4.41 / 4.36	4.77	S10.65 / 10.57	10.92	290 / 292	29:3
$3,4\text{-}(C_3H_7O)_2C_6H_3CH_2CN$	107—108	52	N5.88 / 5.76	6.00	—	—	—	—
$3,4\text{-}(C_4H_9O)_2C_6H_3CH_2CN$	103—104	55	N5.26 / 5.09	5.32	—	—	—	—
$3,4\text{-}(C_3H_7O)_2C_6H_3CH_2COOH$	196—197	68	100.32*** / 100.12	—	—	—	—	—

* d_4^{20} 0.9829, n_D^{20} 1.5020.
** d_4^{20} 0.9982, n_D^{20} 1.4920.
*** By titration with KOH.

TABLE 2 (continued)

Formula	Melting point	Yield (in %)	% Cl found	% Cl calc.	% H found	% H calc.	M found	M calc.
3,4-(C₄H₉O)₂C₆H₃CH₂COOH	170—172	71	99.99* 99.97	—	—	—	—	—
3,4-(C₄H₉O)₂C₆H₃CH₂N(CH₃)₃Cl	218—219	84	N4.50 4.37	4.24	10.70 Cl 10.80	10.77	—	—
2,5-(C₂H₅O)₂C₆H₃CH₂N(CH₃)₃Cl	82—83	92	N5.00 5.06	5.12	12.56 Cl 12.50	12.61	—	—
2,5-(C₂H₅O)₂C₆H₃CH₂N(C₂H₅)₃Cl	89—90	90	4.60 4.52	4.43	11.33 11.30	11.25	—	—
2,5-(CH₃O)₂C₆H₂[CH₂N(CH₃)₃Cl]₂	258—260	92	8.06 8.00	7.93	19.92 20.00	20.11	—	—
2,5-(CH₃O)₂C₆H₂[CH₂N(C₂H₅)₃Cl]₂-1,4	250—252	95	6.56 6.42	6.40	16.08 16.06	16.24	—	—
2,5-(C₂H₅O)₂C₆H₂[CH₂N(CH₃)₃Cl]₂-1,4	278—280	89	7.21 7.03	7.34	18.46 18.59	18.63	—	—
2,5-(C₂H₅O)₂C₆H₂[CH₂N(C₂H₅)₃Cl]₂-1,4	228—229	95	6.11 5.88	6.02	15.08 15.30	15.26	—	—
2,5-(C₃H₇O)₂C₆H₂[CH₂N(CH₃)₃Cl]₂-1,4	272—273	88	6.57 6.68	6.84	17.20 17.28	17.36	—	—
2,5-(C₃H₇O)₂C₆H₂[CH₂N(C₂H₅)₃Cl]₂-1,4	209—211	95	5.54 5.48	5.67	14.32 14.30	14.40	—	—
2,5-(C₄H₉O)₂C₆H₂[CH₂N(CH₃)₃Cl]₂-1,4	244—245	96	6.29 6.34	6.40	16.07 16.16	16.24	—	—
2,5-(C₄H₉O)₂C₆H₂[CH₂N(C₂H₅)₃Cl]₂-1,4	232—234	97	5.46 5.42	5.37	13.56 13.52	13.62	—	—

* By titration with KOH.

LITERATURE CITED

[1] Organic Reactions 1, 84 (1948).

[2] Yu. A. Baskakov and N. N. Mel'nikov, Doklady Akad. Nauk SSSR   97, 453 (1954).

[3] N. N. Mel'nikov and M. V. Prilutskaya, Uch. Trudy Vil'nyussk. Gos. Univ. 7, 205 (1957).

[4] M. V. Prilutskaya and N. N. Mel'nikov, Uch. Trudy Vil'nyussk. Gos. Univ. 7, 229 (1957).

[5] L. Fitsechr and R. Bogert, J. Org. Ch. 4, 71 (1939).

[6] L. Carri and P. Lieberman, C. r. 199, 791 (1934).

[7] O. Gawron, J. Am. Chem. Soc. 71, 744 (1949).

[8] J. Jacini and T. Bacchetti, Gazz. 8, 757 (1951).

[9] French Pat. 695477; British Pat. 347892; C. A. 26, 2997 (1932).

[10] U.S. Pat. 1887396; C. A., 27, 1359 (1933).

[11] M. Shimizu and M. Maki, Pharm. Soc. Japan 71, 958 (1951).

[12] H. Kaufmann and P. Muller, Ber. 51, 123 (1918).

[13] P. Tiemann, Ber. 13, 1123 (1876).

[14] R. Koel, Lieb. Ann. 159, 245 (1872).

[15] K. R. Irani,   C. A. 45, 1974B, (1951).

[16] R. Robinson J. Chem., Soc. 107, 270 (1915).

[17] O. Decker and N. Pschorr, Ber. 37, 3404 (1904).

THE INTERACTION OF ALCOHOLS WITH TRIETHYLHYDROXYSILANES

K. A. Andrianov and V. V. Astakhin

V. I. Lenin All-Union Institute of Electrotechnics

It is known that dialkyl- and diarylhydroxysilanes easily undergo polycondensation with formation of compounds with siloxane bonds.

$$xR_2Si(OH)_2 \longrightarrow (R_2SiO)_x + xH_2O$$

Trialkylhydroxysilanes also react relatively easily according to the equation

$$2R_3SiOH \longrightarrow R_3SiOSiR_3 + H_2O.$$

It was therefore assumed that the reaction between trialkylhydroxysilanes and alcohols does not go in the direction of formation of trialkyl-substituted esters of orthosilicic acid, due to the great susceptibility of trialkylhydroxysilanes to dehydration. The literature contains only indirect references to the possibility of reaction of organohydroxysilanes with alcohols [1, 2]. The possibility of synthesis of organoalkoxysilanes, and in particular of trialkylalkoxysilanes, by direct coupling of alcohols with organohydroxysilanes has not been investigated.

The study of the reaction of triethylhydroxysilane with various alcohols (isopropyl, isobutyl, and amyl) showed that in the absence of catalysts (HCl, H_2SO_4, etc.) triethylhydroxysilanes react with alcohols according to the equation.

$$R'_3SiOH + HOR'' \longrightarrow R'_3SiOR'' + H_2O$$
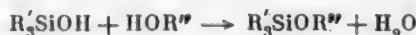
In a secondary reaction a small portion of the triethylhydroxysilane is converted into hexaethyldisiloxane by dehydration.

Reaction of triethylhydroxysilane with the above-mentioned alcohols gives trialkyl-substituted esters of orthosilicic acid in yields of up to 52%. The yield of triethylalkoxysilanes increases with increasing boiling point of the alcohol. This is due to the better conditions for removal from the reaction sphere of the water formed by interaction of the alcohols with triethylhydroxysilane. The properties of the prepared triethylalkoxysilanes are set forth in the table. The method described here may possess preparative value for the synthesis of triethylalkoxysilanes.

EXPERIMENTAL

Reaction of triethylhydroxysilane with isopropyl alcohol. 99 g of triethylhydroxysilane [b.p. 70° (18 mm), n_D^{20} 1.4344] and 180 g of isopropyl alcohol which had been dried over copper sulfate and distilled (b.p. 79°, n_D^{20} 1.3788) were charged into the still of a rectifying column (packed height 600 mm and diameter 21 mm). The column was packed with 3 mm diameter glass rings and connected to the atmosphere through a calcium chloride tube. The reaction mixture was carefully fractionated at 743 mm. Fractions were taken off at such a slow rate that the whole distillation extended over 19 hr. The following fractions were isolated: 1st, 79° (126.7 g), 2nd, 79-163° (56.3 g), 3rd, 163° (45.8 g, yield 35.1%), and residue (30.5 g).

TABLE

Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.
$(C_2H_5)_3SiOC_3H_7$-iso	163° (743)	1.4150	0.8114	53.69	54.30
$(C_2H_5)_3SiOC_4H_9$-iso	185 (763)	1.4192	0.8194	57.95	58.93
$(C_2H_5)_3SiOC_5H_{11}$	209 (741)	1.4269	0.8239	62.93	63.56

The 3rd fraction was triethylisopropoxysilane and it had the following constants:

n_D^{20} 1.4150, d_4^{20} 0.8114, MR 53.69; calc. 54.30.

Found %: C 62.18, 62.11; H 12.73, 12.84; Si 15.41, 15.64; M 176. $C_9H_{22}OSi$. Calculated %: C 62.06; H 12.64; Si 16.09. M 174.

Reaction of triethylhydroxysilane with isobutyl alcohol. A mixture of 99 g triethylhydroxysilane [b.p. 70° (18 mm), n_D^{20} 1.4339] and 222 g isobutyl alcohol which had been dried over copper sulfate and distilled (b.p. 107°, n_D^{20} 1.3963) was subjected to careful fractionation in a rectifying column. The following fractions were separated: 1st 88-107° (45.7 g), 2nd 107° (148.9 g), 3rd 107-185° (19.5 g), 4th 185° (70.1 g, yield 49.7%) and residue 19.4 g).

The 4th fraction was triethylisobutoxysilane and it had the following constants:

n_D^{20} 1.4192, d_4^{20} 0.8194, MR 57.95, calc. 58.93.

Found %: C 63.53, 63.70; H 12.92, 12.90; Si 14.50, 14.57. M 181, 186. $C_{10}H_{24}OSi$ Calculated %: C 63.82; H 12.76; Si 14.89. M 188.

Reaction of triethylhydroxysilane with n-amyl alcohol. A mixture of 49.5 g triethylhydroxysilane [b.p. 70° (18 mm), n_D^{20} 1.4344] and 132 g n-amyl alcohol which had been dried over copper sulfate and distilled (b.p. 136°, n_D^{20} 1.4107) was subjected to careful fractional distillation. The following fractions were isolated: 1st, 90-136° (10.1 g), 2nd 136° (89.7 g), 3rd 136-209° (22.7 g), 4th 209° (38.9 g, yield 51.6%), and residue (10.5 g).

The 4th fraction was triethylamyloxysilane and it had the following constants:

n_D^{20} 1.4269, d_4^{20} 0.8239, MR 62.93; calc. 63.56.

Found %: C 65.51, 65.49; H 13.05, 13.03; Si 13.69, 13.65. M 196. $C_{11}H_{26}OSi$. Calculated %: C 65.34; H 12.87; Si 13.86. M 202.

SUMMARY

1. Triethylhydroxysilane reacts with alcohols with formation of triethylalkoxysilanes.

2. Triethylisopropoxysilane, triethylisobutoxysilane, and triethylamyloxysilane, not previously described in the literature, were prepared and characterized.

LITERATURE CITED

[1] H. Gilman and L.S. Miller, J. Am. Chem. Soc. 73, 2367 (1951).

[2] W.T. Grubb, J. Am. Chem. Soc. 76, 3408 (1954).

METHYLALKOXYCHLOROSILANES

K. A. Andrianov and A. A. Kazakova
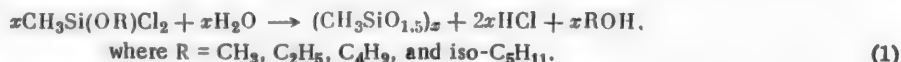
All-Union Electrotechnical Institute

Formation of a solid, infusible, and insoluble product is observed during the preparation of polymethylsiloxanes by hydrolysis of methyltrichlorosilane in aqueous media. The use during hydrolysis of solvents capable of dissolving the products of hydrolysis does not always enable formation of the insoluble products to be avoided. Thus, for example, the hydrolysis of methyltrichlorosilane in a water—toluene medium at 20° and with vigorous stirring also leads to formation of insoluble solids. This shows that hydrolysis of methyltrichlorosilane is accompanied by intensive condensation of the hydrolysis products, with formation of complex compounds. Formation of soluble products of hydrolysis occurs only if alcohols are introduced into the hydrolyzing mixture. Our investigations showed that formation of soluble products by hydrolysis of methyltrichlorosilane necessitates introduction into the aqueous toluene medium of a considerable quantity of an alcohol—about two moles per mole of methyltrichlorosilane. In these ratios butyl and amyl alcohols bring about formation of soluble products; in presence of methyl and ethyl alcohols, insoluble products are formed. We suggest that formation of soluble polymers during hydrolysis of methyltrichlorosilane in a mixture of an alcohol (butyl or amyl), toluene, and water is associated with partial etherification of methyltrichlorosilane by the alcohols with formation of methylalkoxychlorosilanes. In these compounds, the hydrolysis of the alkoxy group linked to silicon proceeds incomparably more slowly than hydrolysis of the chlorine atom; the undesirable intensive chain-branching processes and gelatinization during hydrolysis are thereby avoided.

In this connection, we attempted to study the behavior of methylalkoxychlorosilane during hydrolysis in an aqueous toluene medium. For this purpose we synthesized a series of methylalkoxychlorosilanes by etherification of methyltrichlorosilane with various alcohols according to the general equation

$$CH_3SiCl_3 + nROH \rightleftarrows CH_3SiCl_{3-n}(OR)_n + nHCl,$$
where $R = CH_3, C_2H_5,$ and iso-C_5H_{11}; n = 1 or 2.
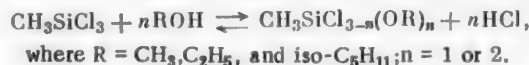
The properties of the preparations are set forth in Table 1. Only the properties of methylethoxychlorosilanes have been described in the literature [1,2]. No information has previously been published about the properties of methoxy-, butoxy- and isoamyloxymethylchlorosilanes.

The isolated chloroethers were subjected to hydrolysis in toluene solution with excess of water at 20-25°. Hydrolysis in each case leads to insoluble trimers:

$$xCH_3Si(OR)Cl_2 + xH_2O \longrightarrow (CH_3SiO_{1.5})_x + 2xHCl + xROH.$$
where $R = CH_3, C_2H_5, C_4H_9,$ and iso-C_5H_{11}. \hfill (1)

The products of hydrolysis of methyldibutoxychlorosilane and methyldiisoamyloxychlorosilane dissolve completely in a mixture of alcohol and toluene. In this case the reaction goes with formation of a linear unbranched polymer:
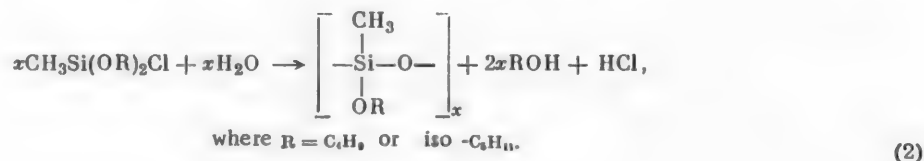
$$xCH_3Si(OR)_2Cl + xH_2O \longrightarrow \begin{bmatrix} CH_3 \\ | \\ -Si-O- \\ | \\ OR \end{bmatrix}_x + 2xROH + HCl,$$
where $R = C_4H_9$ or iso-C_5H_{11}. \hfill (2)

TABLE 1

Compound	Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR found	MR calc.	% C found	% C calc.	% H found	% H calc.	% Si found	% Si calc.	% Cl found	% Cl calc.	Yield (in %)
Methylmethoxy-dichlorosilane	$CH_3SiCl_2(OCH_3)$	79—80° (760)	1.1424	1.3945	30.45	30.11	16.95, 16.50	16.55	4.92, 4.92	4.13	18.68, 18.45	19.31	48.03, 48.11	48.94	43
Methyldimethoxy-chlorosilane	$CH_3SiCl(OCH_3)_2$	93—94 (760)	1.0426	1.3820	31.33	31.38	25.66, 25.89	25.62	6.75, 6.92	6.40	19.20, 19.48	19.92	24.92, 25.09	25.26	38
Methylethoxydi-chlorosilane	$CH_3SiCl_2(OC_2H_5)$	98—101 (760)	1.1037	1.3990	34.86	34.93	23.20, 23.49	22.64	5.20, 5.38	5 03	17.84, 18.04	17.61	44.00, 43.85	44.65	27
Methyldiethoxy-chlorosilane	$CH_3SiCl(OC_2H_5)_2$	127—131 (760)	0.9822	1.3912	40.81	40.69	36.60, 36.23	35.60	8.02, 8.58	7.71	17.50, 17.26	16.61	21.49, 21.77	21.06	23
Methylbutoxydi-chlorosilane	$CH_3SiCl_2(OC_4H_9)$	144—146 (760)	1.0486	1.4138	44.29	44.19	32.70, 32.71	32.08	6.90, 6.73	6.41	14.00, 14.20	14.97	37.58, 38.05	37.96	35
Methyldibutoxy-chlorosilane	$CH_3SiCl(OC_4H_9)_2$	202—204 (760)	0.9398	1.4130	59.61	59.21	49.06, 48.60	48.10	9.08, 9.05	9.35	11.61, 11.81	12.47	15.34, 15.22	15.81	43
Methylisoamyloxy-dichlorosilane	$CH_3SiCl_2(OC_5H_{11})$	56—57 (16)	1.0341	1.4158	48.31	48.69	36.07, 35.95	35.82	7.43, 7.65	6.96	13.78, 13.44	13.93	35.45, 35.80	35.32	25
Methyldiisoamyl-oxychlorosilane	$CH_3SiCl(OC_5H_{11})_2$	105 (20)	0.9283	1.4172	68.90	68.52	52.71, 52.80	52.27	10.09, 10.39	9.90	10.19, 10.46	11.08	13.90, 14.20	14.05	37

When R = CH_3 or C_2H_5 the reaction goes with formation of insoluble products of hydrolysis (as in equation

EXPERIMENTAL

Methylalkoxychlorosilanes were synthesized from methyltrichlorosilane (b.p. 66-66.5°, chlorine content 70.3%) and methyl, ethyl, butyl, and isoamyl alcohols dried over copper sulfate and twice distilled.

Preparation of methylalkoxychlorosilanes. The reaction was run in a three-necked flask fitted with a stirrer, reflux condenser, dropping funnel, and thermometer. The alcohol was added dropwise with stirring to the methyltrichlorosilane. The temperature was not regulated during the addition of the alcohol (the process is exothermic). After the alcohol had been added. the reaction mass was stirred for one hr and then heated at 50-60° for 5-12 hr with stirring. The reaction products were fractionally distilled (usually 2-3 times) in a Favorskii flask for isolation of the pure products.

Methylmethoxydichlorosilane. To 149.46 g methyltrichlorosilane was added dropwise 32.04 g methyl alcohol with stirring. The mixture was stirred one hr at 7-10° and 5 hr. at 50-55°. The 79-81° fraction (62.9 g) was methylmethoxydichlorosilane.

Methyldiisoamyloxychlorosilane. 176.30 g isoamyl alcohol was added dropwise to 149.36 g methyltrichlorosilane. The mixture was stirred one hr at 12-15° and 10 hr at 50-60°. The 105° (20 mm) fraction (91 g) was methyldiisoamyloxychlorosilane.

Other methylalkoxychlorosilanes were similarly synthesized. The properties of the preparations are presented in Table 1.

Hydrolysis of methylalkoxychlorosilanes. A mixture of water and toluene was put into a three-necked flask fitted with stirrer, dropping funnel, and thermometer . A mixture of methylalkoxychlorosilane and toluene was continuously stirred in from the dropping funnel. The reaction mixture was at a temperature of 20-25°. Thereupon the mixture was stirred for another 60-70 min. Ratios of starting components and results of hydrolysis are set forth in Table 2. Similar results were obtained if the order of introduction of reactants was reversed under the same hydrolysis conditions and with the same ratios.

TABLE 2

Ratios of Starting Components and Results of Hydrolysis of Methylalkoxychlorosilanes.

Starting methylalkoxy-chlorosilane	Taken for hydrolysis (in g)			Hydrolysis temperature	Duration (min)		Products of hydrolysis
	chloro-ether	toluene	water		of intro-duction of mixture	stirring of hydrolysis product at 20°	
$CH_3SiCl_2(OCH_3)$	72.52	74.75	149.50	20°	45	60	Insoluble
$CH_3SiCl_2(OC_2H_5)$	79.50	74.80	149.50	20	90	60	
$CH_3SiCl_2(OC_4H_9)$	65.00	52.00	104.00	20	45	60	
$CH_3SiCl_2(OC_5H_{11})$	70.00	52.50	105.00	20	45	60	
$CH_3SiCl(OCH_3)_2$	70.30	74.75	149.50	20	35	60	
$CH_3SiCl(OC_2H_5)_2$	84.30	74.80	149.50	20	60	60	
$CH_3SiCl(OC_4H_9)_2$	56.20	37.40	74.80	20	45	60	Soluble
$CH_3SiCl(OC_5H_{11})_2$	107.00	62.00	124.00	20	50	60	

SUMMARY

1. The following new compounds were synthesized: methylmethoxydichlorosilane, methyldimethoxychlorosilane, methylbutoxydichlorosilane, methyldibutoxychlorosilane, methylisoamyloxychlorosilane, methyldiiso-amyloxychlorosilane.

2. The hydrolysis of methylalkoxychlorosilanes in a mixture of water and toluene at 20° was investigated. It was shown that hydrolysis of methylalkoxydichlorosilanes as well as of methyldimethoxy- and methyldiethoxy chlorosilanes leads to formation of insoluble polymers; hydrolysis of methyldibutoxy- and methyldiisoamyloxy-chlorosilanes gives soluble products.

LITERATURE CITED

[1] M. Kumada, J. Inst. Polytechn. Osaka City, Univ., Ser. C., 2, 139 (1952); C. A. 48, 11303 (1954).

[2] K.A. Andrianov, S.A. Golubtsov, and N.P. Lobusevich, Zhur. Obshchei Khim. 26, 197 (1956).*

Received April 7, 1959
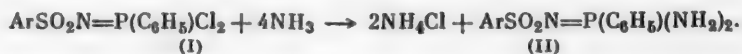
AMMONOLYSIS OF PHENYLDICHLOROPHOSPHAZOSULFONARYLS

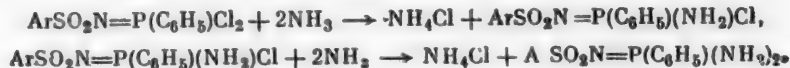V.I. Shevchenko and V.T. Stratienko

Dnepropetrovsk Metallurgical Institute

In the preceding communication [1] reactions of phenyldichlorophosphazosulfonaryls (I) with aniline were described and results of a study of the hydrolysis of phenyldianilinophosphazosulfonaryls were presented.

It was of interest to compare the conditions of preparation and the chemical properties of phenyldianilino-phosphazosulfonaryls with those of ammonia derivatives, and to clarify the influence of the phenyl radical on the mobility of the amino group.

Ammonia behaves unlike aniline in reacting with great facility with phenyldichlorophosphazosulfonaryls with liberation of much heat. Passage of dry ammonia through a benzene solution gives phenyldiaminophosphazo-sulfonaryls (II) in good yields according to the equation

$$ArSO_2N{=}P(C_6H_5)Cl_2 + 4NH_3 \longrightarrow 2NH_4Cl + ArSO_2N{=}P(C_6H_5)(NH_2)_2.$$
$$\text{(I)} \qquad\qquad\qquad\qquad\qquad\qquad\qquad \text{(II)}$$

The following mechanism is suggested for the formation of (II):

$$ArSO_2N{=}P(C_6H_5)Cl_2 + 2NH_3 \longrightarrow NH_4Cl + ArSO_2N{=}P(C_6H_5)(NH_2)Cl,$$
$$ArSO_2N{=}P(C_6H_5)(NH_2)Cl + 2NH_3 \longrightarrow NH_4Cl + A\ SO_2N{=}P(C_6H_5)(NH_2)_2.$$

In contrast, however, to the arylaminolysis reaction [1] the partial amination reaction is not observed to take place. Compounds (II) are colorless crystals, insoluble in ether, benzene, and carbon tetrachloride, easily soluble in acetone and hot alcohol, moderately soluble in boiling water. Phenyldiaminophosphazosulfonaryls have a neutral reaction in aqueous solution and do not titrate with a solution of sodium hydroxide in presence of phenolphthalein; with silver nitrate, however, they give a precipitate of silver salt insoluble in water . In this respect they resemble triaminophosphazosulfonaryls (III) which form monosilver salts of the composition $ArSO_2NAg{-}P(NH_2)_2({=}NH)$ [2]. Like (III), (II) might exist in tautomeric forms in aqueous solution:

$$ArSO_2N{=}P(C_6H_5)(NH_2)_2 \rightleftarrows ArSO_2NH{-}P(C_6H_5)(NH_2)({=}NH) \rightleftarrows$$
$$\rightleftarrows ArSO(OH){=}N{-}P(C_6H_5)(NH_2)({=}NH)$$
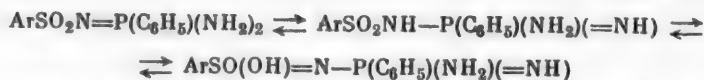
Compounds (II) differ from (III) in being extremely stable to the action of water. Compounds (III) are hydrolyzed in aqueous solutions even in the cold with formation of ammonium salts of diaminoarylsulfonamido-phosphoric acids according to the equation

$$ArSO_2N{=}P(NH_2)_3 + H_2O \longrightarrow ArSO_2N{=}P(NH_2)_2(ONH_4),$$
$$\text{(III)}$$

and (III) are readily hydrolyzed by boiling water to form arylsulfamides

$$ArSO_2N{=}P(NH_2)_3 + 2H_2O \longrightarrow ArSO_2NH_2 + OP(NH_2)_2(ONH_4),$$

On the other hand (II) are not hydrolyzed by water even on prolonged boiling. Consequently the phenyl group attached directly to the phosphorus atom imparts resistance to hydrolysis to phenyldiaminophosphazosulfonaryls.

If we assume the following structures for (II) and (III)
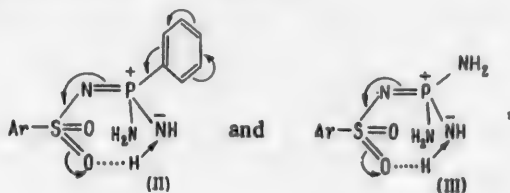
then it appears that the formation of a hydrogen bond in the triamino derivatives (III) and the shift of the electron pairs results in a dipole with a positive charge at the phosphorous, and this favors nucleophilic substitution of the amino group by the hydroxyl ion. In phenyldiaminophosphazosulfonaryls (II) the positive charge at the phosphorus is distributed at the benzene ring due to π-conjugation with the phenyl nucleus, and this hinders attack of the phosphorus by the nucleophilic ion.

Compounds (II) differ from (III) in being hydrolyzed only under rather drastic conditions, for example on heating on a water bath with 0.2 N aqueous sodium hydroxide or hydrochloric acid. Under these conditions (II) are hydrolyzed to arylsulfamides.

In an alkaline medium the hydrolysis goes with evolution of ammonia and formation of arylsulfamide and sodium salt of the amide of phenylphosphinic acid.

$$ArSO_2N=P(C_6H_5)(NH_2)_2 + H_2O \xrightarrow{NaOH} ArSO_2NH_2 + OP(C_6H_5)(NH_2)(ONa) + NH_3$$

It was to be expected that (II) would be hydrolyzed in accordance with the following mechanism:

$$ArSO_2N=P(C_6H_5)(NH_2)_2 + NaOH \longrightarrow ArSO_2NNa-PO(C_6H_5)(NH_2) + NH_3,$$

$$ArSO_2NNa-PO(C_6H_5)(NH_2) + H_2O \longrightarrow ArSO_2NH_2 + OP(C_6H_5)(NH_2)(ONa).$$

This is supported by the fact that triamino-, trianilino- and phenyldianilinophosphazosulfonaryls easily form relatively stable monometallic salts on hydrolysis. Partial hydrolysis of (II) in accordance with the first equation, however, cannot be realized.

Yields, melting points and analytical data of phenyldiaminophosphazosulfonaryls (II) are set forth in the table.

TABLE

Phenyldiaminophosphazosulfonaryls $ArSO_2N = P(C_6H_5)(NH_2)_2$

Ar	Yield (in %)	Melting point	Empirical formula	% N found	% N calc.
C_6H_5	90.7	151—152°	$C_{12}H_{14}O_2N_3SP$	14.26	14.23
o-$CH_3C_6H_4$	94.9	140—142	$C_{13}H_{16}O_2N_3SP$	13.74	13.59
p-$CH_3C_6H_4$	92.6	130—131	$C_{13}H_{16}O_2N_3SP$	13.58	13.59
p-ClC_6H_4	91.6	162—164	$C_{12}H_{13}O_2N_3SPCl$	12.38	12.30
α-$C_{10}H_7$	94.4	149—151	$C_{16}H_{16}O_2N_3SP$	11.84	12.14
β-$C_{10}H_7$	97.2	148—152	$C_{16}H_{16}O_2N_3SP$	12.02	12.14

EXPERIMENTAL

Preparation of phenyldiaminiophosphazosulfonaryls. 0.01 mole of (I) was dissolved in 40 ml of dry benzene and dry ammonia (dried over sodium) was slowly passed for one hr through the solution. The reaction mixture was cooled to 10-15° during the operation. The resulting crystalline precipitate was suction-filtered and washed several times with cold water for removal of ammonium chloride. (II) was purified by crystallization from water or alcohol.

Hydrolysis of phenyldiaminophosphazosulfonaryls in an alkaline medium. To 0.005 mole of (II) was added 25 ml of 0.2 N aqueous sodium hydroxide and the mixture was heated for 30 min on a water bath. After cooling, the precipitated arylsulfamide was separated and the filtrate was evaporated to dryness.

The sodium salt of phenylphosphinamide, remaining after extraction of the dry residue with boiling benzene, was crystallized from dilute (50%) alcohol. Fine, short needles with m.p. 164-165°.

Found %: N 7.83. $C_6H_7O_2NPNa$. Calculated %: N 7.82.

Hydrolysis in an acid medium was carried out in similar fashion. In this case the phosphorus-containing portion, remaining after separation of the arylsulfamide, was not investigated.

SUMMARY

1. Reaction of phenyldichlorophosphazosulfonaryls with ammonia gave phenyldiaminophosphazosulfonaryls.

2. In an alkaline medium phenyldiaminophosphazosulfonaryls are hydrolyzed with formation of ammonia arylsulfamide and sodium salt of phenylphosphinamide.

LITERATURE CITED

[1] V.I. Shevchenko and V.T. Stratienko, Zhur. Obshchei Khim. **29**, 3458 (1959).*

[2] A.V. Kirsanov and E.A. Abrazhanova, Zhur. Obshchei Khim., Supp. II, 1059 (1953).

Received March 6, 1959

---

*Original Russian pagination. See C. B. Translation.

DERIVATIVES OF ACYLACETIC ESTERS

OF THE HETEROCYCLIC SERIES

I. ARYLIDES OF α- AND β-FUROYLACETIC ACIDS

N.S. Vul'fson and V.E. Kolchin

K.E. Voroshilov State Scientific Research Institute
for Organic Intermediates and Dyes

Arylides of β-ketoacids are extensively used as intermediates in the manufacture of a series of azo dyes and also as color-forming components in the manufacture of motion-picture color films for production of a yellow image under the conditions of color development. The literature contains methods for preparation and application of arylides of aceto- [1], benzoyl- [2], indolyl-2- [3] and α-furoylacetic acids [4]. The last-mentioned type has been relatively little studied and nothing has been published about arylides of β-furoylacetic acid.

We set ourselves the task of preparing a series of arylides of α- and β-furoylacetic acids with the aim of comparing their color-photographic and chemical properties.

α- and β-furoylacetic esters were previously prepared by ester condensation from esters of α- and β-furan-carboxylic acids and ethyl acetate in presence of sodium as condensing agent [5-7]. We prepared α- and β-furoyl-acetic esters by condensation of α- and β-furancarboxylic acid chlorides [8,9] with sodium acetoacetic ester followed by ammonolysis of the respective furoylacetoacetic esters with 10% aqueous ammonia at 35-45°. It was observed that in the β-series the reactions of formation of furoyl chloride, furoylacetic ester, and arylides of furoylacetic acid proceed very much more slugglishly and with lower yields than in the α-series.

We prepared β-furancarboxylic acid by the method [9] starting from malic acid; the latter was heated with 20% oleum and thereby converted into coumalic acid. The methyl ester of the latter was brominated at room temperature. The resulting methyl ester of bromocoumalic acid was rearranged with aqueous potassium hydroxide to form the potassium salt of furan-2,4-dicarboxylic acid, which on heating with copper powder was decarboxylated to β-furancarboxylic acid.

Arylides of furoylacetic acids were prepared by the usual method of heating of the corresponding furoylacetic ester with aromatic amine in a solvent. As the amine components we took o-, m-, and p-anisidines and o-, m-, and p-anisidines and o-, m-, and p-amino- benzoic acids. The yields of arylides were increased in some cases by addition of a small quantity of pyridine or triethanolamine. The latter apparently function as enolizing agents and thereby stabilize the yield and facilitate formation of arylide. It should be noted that the yield of expected product is sharply lowered by rise of temperature to 135-145°, especially toward the end of the reaction, apparently due to the thermal instability of the arylides and the occurrence of secondary reactions.

The prepared arylides are colorless crystalline substances, easily soluble in 5% sodium carbonate solution, with a yellow color; in alcohol and dioxane with $FeCl_3$ they give a greenish-brown coloration. Under the conditions of color development with p-diethylaminoaniline they form yellow azomethine dyes.

EXPERIMENTAL

α-Furoylacetic ester. To a mixture (cooled to 6°) of 13 g acetoacetic ester and 39 ml solution of sodium ethoxide (from 4.6 g sodium in 78 ml anhydrous alcohol) was added dropwise 6.5 g α-furoyl chloride in the course

of 20 min, the temperature being held at 10-12°. After the mass had been stirred for a further 30 min at the same temperature, a further 39 ml of sodium ethoxide was added and another 6.5 of α-furoyl chloride was added drop-wise in the course of 20 min. The mass was stirred for 30 min and stood overnight. The sodium derivative of furoylacetoacetic ester was filtered; the precipitate was dissolved in 80 ml water, and 15 ml of 10% ammonia and 5.5 g of ammonium chloride were added. The reaction mass was heated to 40° and shaken for 15 min; the separated layer was extracted with ether; the extract was dried with calcium chloride, the ether was driven off, the residue was distilled in vacuo, and the 120-125° (8 mm) fraction was collected. Yield 83%.

β-Furoylacetic ester was prepared similarly to the isomer. Yield 44% B.p. 105-107° (3 mm).

o-Anisidide of α-furoylacetic acid. 0.005 mole of α-furoylacetic ester, 0.005 mole of o-anisidine, and 15 ml of xylene were heated for 15 min to 145°, and 10 ml solvent was distilled off with stirring. The mixture was then cooled to 90-100° and a further 3-4 ml of solvent was distilled off in vacuo. The residue was washed with ether and recrystallized from aqueous methyl alcohol.

A series of arylides of α- and β-furoylacetic acids was synthesized under similar conditions. Their properties are set forth in the table.

TABLE

Arylides of α- and β-Furoylacetic Acids of the General Formula

$$\text{COCH}_2\text{CONHR}$$
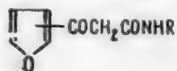
No.	Position of substituent in the furan ring	R	Yield (in %)	Melting point	Found (%)		
					C	H	N
1		o-CH₃OC₆H₄	76	84°	65.10	5.24	5.40
					65.01	5.23	5.32
2	α	P-CH₃OC₆H₄	78	106	64.76	5.23	5 28
					64.80	5.10	5.31
3		м-CH₃OC₆H₄	69	67—68	65.15	4.84	5.30
					64.96	5.05	5.32
4		o-CH₃OC₆H₄	69	116—117	64.88	5.06	5.21
							5.33
5	β	P-CH₃OC₆H₄	72	117—118	64.99	5.34	5.31
					64.83	5.32	5.33
6		м-CH₃OC₆H₄	67	60—61	65.13	4.96	5.31
					65.05	5.16	5.28
7		o-HOOCC₆H₄	54	98—99	61.25	4.09	4.98
					61.33	4.19	5.13
8	α	p-HOOCC₆H₄	56	216	—	—	5.07
							4.91
9		м-HOOCC₆H₄	57	203	61.18	4.02	4.97
							4.98
10		o-HOOCC₆H₄	50	146—147	—	—	4.82
							4.76
11	β	м-HOOCC₆H₄	54	214	61.68	3.98	4.85
					61.82	4.04	4.92
12		p-HOOCC₆H₄	49	228	—	—	4.90
							5.12

Note. Substances 1-6: $C_{14}H_{13}O_4N$. Calculated %: C 64.86; H 5.050; N 5.40. For substances 7-12: $C_{14}H_{11}O_5N$. Calculated %: C 61.53; H 4.06; N 5.12.

SUMMARY

1. Condensation of α- and β-furoyl chloride with sodium acetoacetic ester and subsequent ammonolysis gave α - and β -furoylacetic esters.

2. Interaction of α- and β - furoylacetic esters with o-, m-,and p-anisidines and with o-, m-,and p-aminobenzoic acids gave the corresponding arylides. Under color-developing conditions with p-diethylaminoaniline, the products gave yellow azomethine dyes.

LITERATURE CITED

[1] Bios Report 986, 17, 19-23, 26; West German Patent 900781.

[2] J. Soc. Dyers Col. 64, 106-108 (1948); French Patent 974528; West German Patent 843405.

[3] German Patent 675612; Belgian Patent 512799; French Patent 848247; U.S. Patent 2264213.

[4] A. Cerniani, G. Cordella, Ricerca sci. 26, 2721 3352 (1956); C. A., 51, 15951, 15133 (1957).

[5] S.S. Sandelin, Ber. 33, 492 (1900).

[6] R. Carreras Linares, D. Carreras Bayes, J. Palleiro Cardona, Publ. inst. quim. "Alonso Barba" (Madrid), 4, 310 (1950); C. A. 46, 8082 (1952).

[7] T. Kubota, T. Matsuura, Chem. and Ind. 23, 521 (1956).

[8] H. Kauffman, Ber. 37, 2951 (1904).

[9] H. Gilman, R. Burtner, J. Am. Chem. Soc. 55, 2905 (1933).

INTERACTION OF 6-CHLOROMETHYLQUINOLINE
WITH SULFUR COMPOUNDS

B.P. Lugovkin

All-Union Scientific Research Institute for Industrial Safety
All-Union Central Council of Trade Unions, Kazan

In continuation of our earlier studies of the replacement of the labile halogen atom of 6-chloromethyl-quinoline by various functional groups [1], we have investigated the interaction of 6-chloromethylquinoline with potassium thiocyanate and selenocyanate and with primary and secondary sodium sulfides.

6-Chloromethylquinoline reacts with facility with potassium thiocyanate and selenocyanate in methanol solution with formation of 6-thiocyanomethylquinoline (I) and 6-selenocyanomethylquinoline (II) in quantitative yields. Both of these compounds are crystalline.
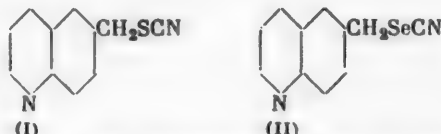
Hydrolysis of thiocyanate (I) with concentrated hydrochloric acid at room temperature leads to 6-mercapto-methylquinoline (III) and carbon dioxide. The mercaptan was identified though the product of its oxidation in the form of diquinolyl-6,6'-dimethyl disulfide (IV); yield 35%.
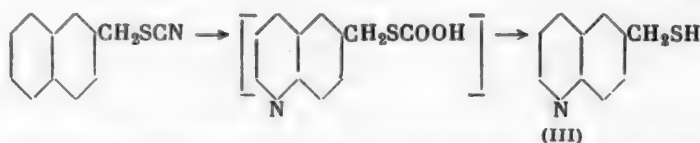
Hydrolysis of the nitrile group of compound (II) is accompanied by formation mainly of polymeric products and by release of carbon dioxide. In addition, diquinolyl-6,6'-dimethyl diselenide (V) was isolated in crystalline form in 26% yield. The diselenide was evidently formed by oxidation of quinolyl-methylselenomercaptan.

Reaction of 6-chloromethylquinoline with primary sodium sulfide in ethanol solution gave 6-mercaptomethyl-quinoline (III) in the form of an oily liquid which is slowly oxidized by atmospheric oxygen to the corresponding disulfide (IV). The mercaptan was identified as the picrate.

Oxidation of the mercaptan with iodine in an alkaline medium gave diquinolyl-6,6'-dimethyl disulfide (IV). The latter is a crystalline substance; yield 63%.
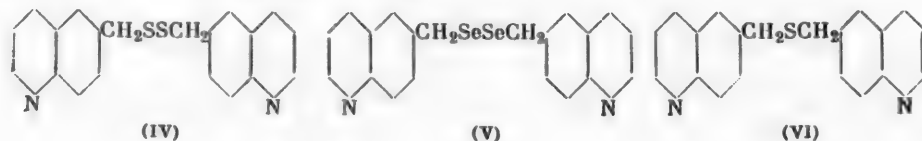
Reaction of 6-chloromethylquinoline with secondary sodium sulfide in methanol solution gave diquinolyl-6,6'-dimethyl sulfide (VI) in crystalline form; the yield was quantitative.

All of the prepared substances (I-VI) were characterized in the form of picrates and dipicrates respectively.

EXPERIMENTAL

6-Thiocyanomethylquinoline (I). A solution of 1.6 g of potassium thiocyanate in 7 ml of methanol was run into 2.2 g of chloro compound in 3 ml of methanol. The mixture was heated on a water bath, with boiling, for 5 min (KCl was precipitated). Dilution with water (50 ml) led to separation of an oily liquid which soon crystallized. 2.38 g (96%) of thiocyanate was obtained in the form of light-yellow crystals with m.p. 98°; recrystallization from benzene gave colorless crystals with m.p. 104-104.5°.

The compound is soluble in methanol, ethanol, acetone, chloroform, and benzene, less readily soluble in ether and hot water.

Found %: S 16.00 $C_{11}H_8N_2S$. Calculated %: S 16.03.

Picrate: prepared in hot alcohol as light-yellow crystals with m.p. 222°. Soluble in alcohol and glacial acetic acid.

Found %: S 7.12. $C_{17}H_{11}O_7N_5S$. Calculated %: S 7.49.

Hydrolysis of the thiocyanate. 2.42 g of the compound was dissolved in 25 ml of hydrochloric acid (d 1.19). After 7-days' standing (in a closed test tube fitted with an exit tube) carbon dioxide came off ($BaCO_3$ precipitate). The mixture was diluted with water (25 ml), neutralized with 50% potassium hydroxide solution until weakly alkaline, and extracted with chloroform. After the solvent had been distilled off, 2 ml of 2 N potassium hydroxide solution was added to the oily liquid (III) followed by 0.1 N aqueous iodine until the color was yellow. The resulting precipitate was extracted with benzene (10 ml). 0.73 g of disulfide was obtained with m.p. 150-151° (polymeric product in the tube). Recrystallization gave nearly colorless crystals with m.p. 153°. A mixture with authentic disulfide melted without depression; m.p. 153°.

Dipicrate: m.p. 234°.

Found %: S 18.39. $C_{20}H_{16}N_2S_2$. Calculated %: S 18.42.

6-Selenocyanomethylquinoline (II). 0.97 g of potassium selenocyanate dissolved in 3 ml of methanol was run into 1.1 g of chloro compound in 3 ml of methanol. KCl quickly came down. The mixture was heated on a water bath, with boiling of the solution for 5 min. Dilution with water (50 ml) brought down a finely crystalline precipitate. 1.4 g (91.5%) of selenocyano derivative was obtained as light-yellow crystals with m.p. 142°; colorless crystals from methanol with m.p. 146°.

Soluble in methanol, ethanol, acetone, chloroform, and benzene, less readily soluble in ether, insoluble in water.

Found %: Se 32.38. $C_{11}H_8N_2Se$. Calculated %: Se 31.97.

Picrate: yellow crystals with m.p. 211°. Soluble in alcohol and glacial acetic acid.

Found %: Se 16.20. $C_{17}H_{11}O_7N_5Se$. Calculated %: Se 16.59.

Hydrolysis of the selenocyano derivative. 1.4 g of the substance was dissolved in 25 ml of hydrochloric acid (d 1.19); a dark-red amorphous solid soon came down. After 5-days' standing the reaction mixture gave carbon dioxide ($BaCO_3$ test). The mixture was diluted with water (25 ml), filtered (weight of precipitate 0.2 g), neutralized with 50% potassium hydroxide solution until weakly alkaline and extracted with chlorform. After the solvent had been distilled off, the solid residue was extracted with benzene (5 ml). 0.43 g of impure crystals was extracted (polymer in container); recrystallization gave 0.33 g of diselenide with m.p. 139°. The m.p. rose to 140° on recrystallization from methanol.

The compound dissolves on heating in methanol, ethanol, acetone and benzene; it dissolves easily in chloroform in the cold, with difficulty in ether; insoluble in water and aqueous caustic alkalies.

Found %: Se 35.11. M 448.1 (Rast). $C_{20}H_{16}N_2Se_2$. Calculated %: Se 35.73; M 442.14.

The diselenide resists attack by aqueous caustic alkali solutions at room temperature. The original substance is recovered after periodic shaking with 50% potassium hydroxide solution for a week.

Dipicrate: prepared in glacial acetic acid; yellow crystals with m.p. 215°. Soluble in glacial acetic acid, soluble with difficulty in alcohol.

Found %: Se 16.97. $C_{32}H_{22}O_{14}N_8Se_2$. Calculated %: Se 17.55.

6-Mercaptomethyldiquinoline (III). 0.65 g of primary sodium sulfide* in 20 ml anhydrous ethanol (in the form of a suspension) was added to 1.5 g of the chloro compound in 3 ml of anhydrous ethanol. The mixture was heated on a water bath with boiling of the solution for 15 min. An oil separated on dilution with water (100 ml); after extraction with ether, drying with sodium sulfate, and distillation of the solvent, a light-yellow, oily liquid was obtained. Weight 1.35 g; the yield of mercaptan, based on the picrate isolated, was 1 g (67.5%).

The compound dissolves readily in ether and other organic solvents; it is less easily soluble in 2 N caustic alkali solution.

Picrate: 0.23 g of substance in 1 ml alcohol was heated with 0.4 g picric acid in 1.5 ml alcohol. 0.4 g picrate was obtained as yellow-greenish crystals with m.p. 239° (after washing in hot glacial acetic acid). Sparingly soluble in alcohol and glacial acetic acid.

Found %: S 7.53. $C_{16}H_{12}O_7N_4S$. Calculated %: S 7.94.

Crystals of the disulfide gradually separated (m.p. 153°) when the mercaptan had been kept in a desiccator for a month.

Diquinolyl-6,6'-dimethyl disulfide (IV). To 0.9 g of mercaptan was added 2 ml of 2 N potassium hydroxide solution followed by 0.1 N aqueous iodine solution until the color was yellow. The deposited solid was recrystallized from methanol; 0.56 g (62.9%) of disulfide was obtained. M.p. 153° (after recrystallization from benzene).

The compound dissolves on heating in methanol, ethanol, acetone, and benzene; it is easily soluble in chloroform in the cold, insoluble in water and aqueous caustic alkali solution. Unlike the mercaptan it is sparingly soluble in ether.

Found %: S 18.35. M 349.7 (Rast). $C_{20}H_{16}N_2S_2$. Calculated %: S 18.43. M 348.34.

The disulfide resists the action of alkalies at room temperature. The original compound is recovered after periodic shaking with 50% potassium hydroxide solution for a week.

The dihydrochloride could not be isolated after hydrogen chloride had been passed into a solution of the disulfide in anhydrous ethanol or acetone.

Dipicrate: prepared in hot glacial acetic acid; yellow crystals melting at 233-234°. A mixture with the picrate of the mercaptan melted with depression (m.p. 226-227°). Soluble in glacial acetic acid, sparingly soluble in alcohol.

Found %: S 8.01. $C_{32}H_{22}O_{14}N_8S_2$. Calculated %: S 7.96.

Diquinolyl-6,6'-dimethyl sulfide (VI). To 1.7 g of chloro compound in 3 ml methanol was added 1.2 g of enneahydrated secondary sodium sulfide dissolved in 10 ml methanol. The mixture was heated on a water bath with boiling of the solution for 15 min. A thick liquid came down on dilution with water (50 ml). Extraction with chloroform gave 1.25 g (82.8%) of thioether. Colorless crystals with m.p. 85° after recrystallization from a mixture of benzene (1.5 ml) and light gasoline (2 ml).

Soluble in alcohol, acetone, benzene, and chloroform, less easily soluble in ether and hot water, poorly soluble in benzine.

Found %: S 10.18. $C_{20}H_{16}N_2S$. Calculated %: S 10.15.

Passage of hydrogen chloride into a solution of the thioether in anhydrous acetone did not lead to separation of the dihydrochloride.

Dipicrate: light-yellow crystals with m.p. 249° (after washing with hot glacial acetic acid). Sparingly soluble in alcohol and glacial acetic acid.

---

*Prepared by saturation with dry hydrogen sulfide of an alcoholic solution of sodium ethoxide (0.8 g metallic sodium in 20 ml anhydrous alcohol), followed by precipitation with anhydrous ether.

Found %: S 4.46 C$_{32}$H$_{22}$O$_{14}$N$_{6}$S. Calculated %: S 4.14.

SUMMARY

1. Reactions of 6-chloromethylquinoline with potassium thiocyanate and selenocyanate and with primary and secondary sodium sulfides were studied.

2. The following were synthesized: 6-selenocyanomethylquinoline, 6-mercaptomethylquinoline, diquinolyl-6,6'-dimethyl disulfide, and diquinolyl-6,6'-dimethyl sulfide. Their chemical properties were examined.

LITERATURE CITED

[1] B.P. Lugovkin, Zhur. Obshchei Khim. 26, 1733 (1956);* 27, 529 (1957); 29, 1350 (1959).*

*Original Russian pagination. See C. B. Translation.

PHENYLTETRAFLUOROPHOSPHORANE AND ITS DERIVATIVES

L. M. Yagupol'skii and Zh. M. Ivanova

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR

Very few compounds containing the grouping—C—P—F are known at the present time. Only the alkyl esters of methylphosphonofluoridic acid have been studied, some of which have proved to be highly toxic compounds (Sarin, Soman)[1, 2]. The alkylated amides of alkylphosphonofluoridic acids and the difluorides of alkylphosphonic acids[3], as well as the fluorides of methylalkylphosphinic acids[4], have been described very recently.

Having undertaken a study of compounds containing the grouping C—P—F, we decided to prepare phenyltetrafluorophosphorane and a number of its derivatives. With this in mind we reacted phenyltetrachlorophosphorane with antimony trifluoride.

$$C_6H_5PCl_4 + SbF_3 \longrightarrow C_6H_5PF_4 + SbCl_3$$

p-Tolyltetrafluorophosphorane and p-chlorophenyltetrafluorophosphorane were obtained in a similar manner.

Zinc fluoride can also be used to replace the chlorine in aryltetrachlorophosphorane compounds by fluorine. However, reaction is less vigorous here. The yield of aryltetrafluorophosphorane compound is 35 to 40%.

The reaction of phenylphosphonous dichloride with antimony trifluoride gave phenyltetrafluorophosphorane, instead of the expected phenylphosphonous difluoride.

$$3C_6H_5PCl_2 + 4SbF_3 \longrightarrow 3C_6H_5PF_4 + 2Sb + 2SbCl_3$$

Metallic antimony was isolated in 92% of the theoretical yield. Apparently, phenylphosphonous difluoride is a very powerful reducing agent. It is interesting to mention that phenylphosphonous dichloride does not reduce antimony trichloride to the metal even when the mixture is refluxed for an hour.

Phenyltetrafluorophosphorane and its derivatives are colorless liquids that fume in the air and etch glass. They are readily soluble in ether, benzene, petroleum ether, carbon tetrachloride, and dioxane. The compounds react with water and with alcohols with the evolution of heat. Complete hydrolysis with water yields arylphosphonic acids and hydrofluoric acid.

In contrast to phenyltetrachlorophosphorane, phenyltetrafluorophosphorane does not react with dry sulfur dioxide, even when heated to 100°, to give the phenylphosphonic difluoride. For this reason, the phenylphosphonic difluorides were obtained from the corresponding dichlorides using zinc fluoride to replace the chlorine by fluorine. Antimony trifluoride is not suitable for this purpose, since the antimony trichloride formed as a result of the exchange has a boiling point that lies close to the boiling points of the arylphosphonic difluorides. The arylphosphonic difluorides are colorless liquids that are readily soluble in all organic solvents. They are much more resistant to the action of atmospheric moisture than the aryltetrafluorophosphoranes; their specific gravities are somewhat lower, while their boiling points are approximately 50° higher than is true of the corresponding aryltetrafluorophosphoranes.

A summary of the obtained compounds, their constants, and their analysis data, is given in Tables 1 and 2.

When benzene solutions of either aryltetrafluorophosphoranes or arylphosphonic difluorides were mixed with a benzene solution of aniline, followed by distilling off the benzene without protection from atmospheric moisture,

TABLE 1

Aryltetrafluorophosphoranes of Type p-$RC_6H_4PF_4$

R	Boiling point at 760 mm	Yield (in %)	d_{20}^{20}	Empirical formula	% F		% P	
					found	calc.	found	calc.
H	133—134°	66	1.3839	$C_6H_5PF_4$	41.70, 40.83	41.30	16.56, 16.46	16.85
CH_3	161—162	62	1.3334	$C_7H_7PF_4$	38.71, 38.68	38.38	15.66, 15.75	15.67
Cl	163—164	61	1.5141	$C_6H_4PF_4Cl$	34.43, 34.59	34.79	14.20, 14.30	14.19

TABLE 2

Arylphosphonic Difluorides of Type p-$RC_6H_4POF_2$

R	Boiling point at 760 mm	Yield (in %)	d_{20}^{20}	Empirical formula	% F		% P	
					found	calc.	found	calc.
H	186—187°	90	1.2982	$C_6H_5OPF_2$	23.36, 23.54	23.46	19.18, 19.27	19.14
CH_3	207—209	72	1.2781	$C_7H_7OPF_2$	22.05, 21.46	21.62	17.68, 17.55	17.61
Cl	211—213	93	1.3381	$C_6H_4OPF_2Cl$	19.21, 19.17	19.33	15.81, 16.20	15.78

we obtained aniline salts of arylphosphonofluoridic acids of type: $ArP(O)FOC_6H_5\overset{+}{N}H_3$.

These salts are quite stable compounds and can be recrystallized from water. Aniline and carbon dioxide are liberated when they are treated with a saturated water solution of potassium carbonate, and the potassium salt of phenylphosphonofluoridic acid is formed. The aniline salt of phenylphosphonofluoridic acid is reprecipitated if aniline hydrochloride is added to a water solution of the potassium salt.

$$C_6H_5P(O)FO^-C_6H_5\overset{+}{N}H_3 \underset{C_6H_5NH_2 \cdot HCl}{\overset{K_2CO_3}{\rightleftarrows}} C_6H_5P(O)FOK$$

The aniline salts of the arylphosphonofluoridic acids are colorless crystalline compounds, readily soluble in alcohol at 20°, and in water and acetone when heated, and difficultly soluble in benzene, ether, and petroleum ether.

EXPERIMENTAL

Phenyltetrafluorophosphorane. Both the yield and the purity of phenyltetrafluorophosphorane are strongly dependent on the preparation conditions. For this reason a detailed description of the apparatus and method of operation is given below, making it possible to run the synthesis with the complete exclusion of atmospheric moisture. Into a 100-ml Claisen flask 1 is charged 10.3 g of phenylphosphonous dichloride. A stream of dry chlorine is passed into the flask through tube 2 (see figure). When the absorption of chlorine ceases and solid phenyltetrachlorophosphorane has been formed, tube 2 is lifted out of rubber sleeve 3, the sleeve clamped with a Mohr clamp, then tube 2 with stopper 5 is removed, and a flask containing 15.7 g of antimony trifluoride is inserted on stopper 4. The antimony trifluoride is added in small portions by opening and closing the Mohr clamp. The reaction is vigorous and a large amount of heat is evolved. The Claisen flask is cooled occasionally in a mixture of water and ice. The reaction is run with the adapter stopcock 6 closed. When reaction is ended, the rubber connection on the calcium chloride tube is clamped shut, the stopcock is opened, a water-jet pump is connected to distributing receiver 8, and the reaction product is distilled. At the start of distillation, in order to remove the hydrofluoric

TABLE 3

Arylamine Salts of Arylphosphonofluoridic Acids of Type $p\text{-}RC_6H_4P\overset{O}{\underset{ONH_3C_6H_4-R'-p}{\diagdown F}}$

R	R'	Melting point	Empirical formula	% F found	% F calc.	% P found	% P calc.	% C found	% C calc.	% H found	% H calc.
H	H	173—174°	$C_{12}H_{13}O_2NPF$	7.82, 7.57	7.52	5.85, 5.76	5.53				
H	CH_3	168—169	$C_{13}H_{15}O_2NPF$	7.15, 6.94	7.10	5.15, 5.26	5.24	58.26, 58.40	58.42	5.89, 5.65	5.65 *
Cl	CH_3	155—157	$C_{13}H_{14}O_2NPFCl$	6.67, 6.03	· 6.31						
CH_3	H	133—135	$C_{13}H_{15}O_2NPF$	6.77, 6.84	7.12						

* This compound was analyzed in the Microanalysis Laboratory of the Institute of Hetero-organic Compounds of the Academy of Sciences of the USSR.

acid formed as the result of glass etching from the system, Claisen flask 7 is not cooled. Then flask 7 is cooled to -50 to -60°, and the phenyltetrafluorophosphorane is distilled at the vacuum of the water-jet pump. When distillation is done, the adapter stopcock is closed, the vacuum disconnected, and air is carefully bled into the system through a tube filled with phosphorus pentoxide. Then the distillation is continued at atmospheric pressure. The pure compound is collected in a receiver with a stopcock, from which the substance is removed in a stream of dry carbon dioxide; yield 7.0 g. The other aryltetraphosphoranes are obtained in a similar manner.

Phenylphosphonic difluoride. A charge of 7.3 g of phenylphosphonic dichloride is placed in a Claisen flask, and then 4.6 g of zinc fluoride is added. A heating up and frothing of the liquid occurs within several minutes. The substance is distilled at atmospheric pressure; yield 5.5 g. The other arylphosphonic difluorides are obtained in a similar manner.
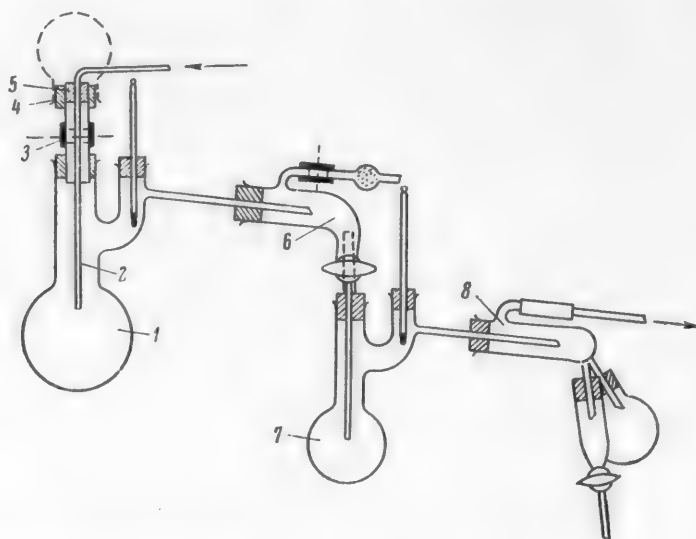
Aniline salt of p-tolylphosphonofluoridic acid. Aniline (8.1 g) is added to 4.4 g of p-tolyltetrafluorophosphorane, and the reaction mixture is allowed to stand overnight. Then the benzene is distilled off using a water-jet pump, without protection from atomospheric moisture. The solid residue is transferred to a glass filter, where the product is washed with benzene and ether, followed by recrystallization from water; yield 3.2 g. The aniline and toluidine salts of the other arylphosphonofluoridic acids are obtained in a similar manner.

SUMMARY

Some aryltetrafluorophosphoranes and the difluorides of phenyl-, p-tolyl-, and p-chlorophenylphosphonic acid were synthesized, and their properties were described.

LITERATURE CITED

[1] M. Sartori, Uspekhi Khim. 23, 62 (1954).

[2] B. C. Saunders, Some Aspects of the Chemistry and Toxic Action of Organic Compounds Containing Phosphorus and Fluorine (Cambridge, 1957) pp. 93, 94.

[3] A. I. Razumov, O. A. Mukacheva and E. A. Markovich, Zhur. Obshchei Khim. 28, 194 (1958).*

[4] T. P. Dawson and K. C. Kennard, J. Org. Chem. 22, 1671 (1957).

*Original Russian pagination. See C. B. Translation.

SPATIAL STRUCTURE AND REACTIVITY

XV. INTERACTION OF SEPARATED ATOMIC GROUPINGS BASED ON DATA OF INVESTIGATING THE KINETICS OF REACTION OF AMINO DERIVATIVES OF TOLAN WITH p-NITROBENZOYL CHLORIDE AND PICRYL CHLORIDE

L. M. Litvinenko and N. F. Levchenko

Kharkov State University

Based on a study of the kinetics of reaction of amino and aminonitro drivatives of biphenyl and trans-stilbene with p-nitrobenzoyl chloride and picryl chloride in benzene solution, it was shown by us in an earlier paper of this series [1] that the molecular system of stilbene, in which the benzene rings are separated by an ethylene bridge, is a poorer transmitter of electronic effects (from one ring to the other) than the biphenyl system, where the benzene rings are linked directly.

In this paper we give the results of investigating the kinetics of reaction of p-nitrobenzoyl chloride and picryl chloride with similar tolan derivatives, and specifically, with 4-aminotolan (I) and 4-amino-4'-nitrotolan (II), under conditions completely identical with the previous.

A study of the reactivity of (I) and (II) makes it possible to determine whether the influence exerted by the 4'-substituent on the reacting group is transmitted better by the stilbene system, in which the benzene rings are connected by an ethylene bridge, or by the tolan system, where the two benzene rings are linked by an acetylene bridge.

The results obtained here also answer to a certain degree the question of which of the two types of bonds— double or triple — is the better conductor of the electronic effects that influence a chemical process.

EXPERIMENTAL

I. Preparation and purification of starting materials. Benzene, p-nitrobenzoyl chloride [2] and picryl chloride [1] were purified as indicated earlier.

4-Aminotolan was synthesized by the method described by us earlier [3], and was purified further by recrystallization first from dilute (2:1) methanol, and then repeatedly (6—7 times) from benzene. The compound, after drying in a vacuum oven at 65° for 1 hr*, had m.p. 128—129°.

4-Amino-4'-nitrotolan (II) was synthesized by the earlier described method [3], and was purified further by recrystallization from ethanol (once; activated carbon), and then from chlorobenzene (3 times). The crystals, after washing with a little benzene, were dried in a vacuum oven at 100° for 6 hr. M.p. 204°.

---

*The substance gradually turns yellow if dried for a longer time, or at a higher temperature.

TABLE 1

Kinetics of Reaction of 4-Aminotolan with p-Nitrobenzoyl Chloride. a = 0.0025M; b = 0.005M

25°				50°			
t_i(in min)	yield (in %)	k_i (in liter/ mole/sec)	n_i	t_i(in min)	yield (in %)	k_i (in liter/ mole/sec)	n_i
20	19.9	0.0417	2	8	22.6	0.126	2
36	30.2	0.0403	2	13	31.3	0.121	2
60	41.7	0.0400	2	25	46.3	0.119	2
100	54.5	0.0402	2	37	55.6	0.117	2
170	67.5	0.0410	2	70	70.5	0.118	2
$K_{25°} = 0.0406 \pm 0.0006$				$K_{50°} = 0.120 \pm 0.003$			

E = 8300 cal/mole; log A = 4.69; $\Delta S^{\neq}$ −39.1 cal/deg · mole.

TABLE 2

Kinetics of Reaction of 4-Amino-4'-nitrotolan with p-Nitrobenzoyl Chloride. a = 0.0025M; b = 0.005M

25°				50°			
t_i (in min)	yield (in %)	k_i (in liter/ mole/sec)	n_i	t_i(in min)	yield (in %)	k_i (in liter/ mole/sec)	n_i
60	16.6	0.0111	2	18	14.7	0.0331	2
100	23.7	0.0104	2	37	25.2	0.0315	2
167	32.4	0.00961	2	70	37.6	0.0297	2
303	46.0	0.00943	2	127	51.1	0.0284	2
718	67.0	0.00949	2	243	67.3	0.0292	2
$K_{25°} = 0.0100 \pm 0.0005$				$K_{50°} = 0.0304 \pm 0.0013$			

E = 8500 cal/mole; log A = 4.24; $\Delta S^{\neq}$ −41.2 cal/deg · mole

It is interesting to mention that an alcohol solution of (II) has an intense red color (the color is also dark red in the crystalline state), whereas benzene and chlorobenzene solutions are light yellow. It seems to us that this is evidence that in a polar solvent like alcohol, the color of a given compound is to a large extent determined by exomolecular reaction forces. The latter, as was shown by Izmail'skii [5, 6], is quite characteristic for compounds that have a similar structure.

II. Method of kinetic measurements and results. The method used to measure the reaction rates, and also the methods used to calculate the bimolecular rate constant, activation energy (E), frequency factor (A) and activation entropy (ΔS *), were described earlier [1]. In all of the experiments the initial concentration of p-nitrobenzoyl chloride or picryl chloride (a) was always half the initial concentration of the amine (b).

The numerical data obtained for the reaction of amino derivatives of tolan are given in order in Tables 1—4, where the following designations apply: k_i and $\underline{k}$ are respectively the average values of the rate constant: 1) for a given time t_i with number of measurements n_i, and 2) for all Σn_i measurements. In these tables, the average values of the reaction yield for n_i measurements are given in the second column.

The principal data on the kinetics of the reactions studied by us in the present paper, and also the values of some of the constants for reactions studied by us earlier, are summarized in Table 5.

From the data in Tables 3 and 4 it can be seen that the rate constant for the reaction of amino derivatives of tolan with picryl chloride decreases somewhat with time. Because of the lack of availability of the indicated amines, we didn't have sufficient amounts of them to permit making a study of the reasons for this phenomenon, but it is possible to assume that because of the high unsaturation and the specific traits of the spatial structure of

TABLE 3

Kinetics of Reaction of 4-Aminotolan With Picryl Chloride a = 0.0050M; b = 0.01m

	25°				50°		
t_i (in min)	yield (in %)	k_i (in liter/mole/sec)	n_i	t_i (in min)	yield (in %)	k_i (in liter/mole/sec)	n_i
51	21.0	0.00872	2	14	21.8	0.0344	2
75	26.8	0.00820	2	30	35.0	0.0310	2
108	34.6	0.00821	2	50	47.1	0.0308	2
164	44.4	0.00818	2	65	53.8	0.0310	2
245	54.3	0.00813	2	120	67.7	0.0302	2
446	67.9	0.00796	2				

$$K_{25°} = 0.00823 \pm 0.00016 \qquad\qquad K_{50°} = 0.0315 \pm 0.0011$$

E = 10,300 cal/mole; log A = 5.45; $\Delta S^{\#}$ = -35.6 cal/deg · mole.

TABLE 4

Kinetics of Reaction of 4-Amino-4'-Nitrotolan With Picryl Chloride a = 0.005 M; b = 0.01 M

	25°				50°		
t_i (in min)	yield (in %)	k_i (in liter/mole/sec)	n_i	t_i (in min)	yield (in %)	k_i (in liter/mole/sec)	n_i
220	19.9	0.00189	2	65	22.0	0.00750	2
368	28.9	0.00185	2	117	32.3	0.00704	2
720	42.6	0.00173	2	220	46.5	0.00683	2
1293	55.4	0.00161	2	410	61.2	0.00665	2

$$K_{25°} = 0.00177 \pm 0.00010 \qquad\qquad K_{50°} = 0.00701 \pm 0.00029$$

E = 10,600 cal/mole; log A = 4.98; $\Delta S^{\#}$ = -37.8 cal/deg · mole.

amino derivatives of tolan, the kinetics of their reaction with picryl chloride is influenced to some degree either by the possible formation of a molecular compound between the two reaction components (see [1, 4]) or by the factors of exomolecular association of like molecules of amino derivatives [5, 6] (see [1]). However, even if these effects are present, their role is small, and consequently they can exert very little influence on the conclusions made in the present paper.

Some of the experiments, made with various initial concentrations of the starting components, revealed that the rate constants of the investigated reactions, the same as had been established earlier for similar cases [7—10], hardly change with dilution. Thus, for example, for the reaction of 4-aminotolan with picryl chloride, at a = 0.0025 and b = 0.005, $K_{25°}$ = 0.00835 liter/mole·sec, while at a = 0.005 and b = 0.01, $K_{25°}$ = 0.00823 liter/mole·sec.

DISCUSSION OF RESULTS •

A comparison of the results, obtained in studying the reaction of aniline, 4-aminotolan, 4-aminostilbene, and 4-aminobiphenyl with the two electrophilic reagents, reveals that in their electron-acceptor effect, p-substituents introduced into the aniline molecule can be arranged in the following order: $C_6H_5 < C_6H_5-CH=CH-$ $C_6H_5-C\equiv C-$.

Using the ratios of the rate constants for the reactions of the monosubstituted and disubstituted derivatives, i.e., $\dfrac{K_I}{K_{II}}$ (factor f), it is possible to give (the same as we had done earlier [1]) a quantitative estimate of the con-

---

• See Summary, Table 5.

TABLE 5

Summary Data on the Kinetics of Reaction of Amines With p-Nitrobenzoyl Chloride and Picryl Chloride*

Amine	Electrophilic agent**	$K_{25°}$	$K_{50°}$	E	log A	$\Delta S^{\ddagger}$
$C_6H_5-C\equiv C-C_6H_4-NH_2$	PNBC	0.0406 ± 0.0006	0.120 ± 0.003	8300	4.69	−39.1
	PC	0.00823 ± 0.00016	0.0315 ± 0.0011	10300	5.45	−35.6
$O_2N-C_6H_4-C\equiv C-C_6H_4-NH_2$	PNBC	0.0100 ± 0.0005	0.0304 ± 0.0013	8500	4.24	−41.2
	PC	0.00177 ± 0.00010	0.00701 ± 0.00029	10600	4.98	−37.8
$C_6H_5-CH=CH-C_6H_4-NH_2$	PNBC	0.280 ± 0.012	0.755 ± 0.012	7600	5.01	−37.7
	PC	0.0619 ± 0.0020	0.222 ± 0.007	9800	5.96	−33.3
$O_2N-C_6H_4-CH=CH-C_6H_4-NH_2$	PNBC	0.0573 ± 0.0032	0.126 ± 0.005	6000	3.18	−46.0
	PC	0.0121 ± 0.0005	0.0428 ± 0.0009	9700	5.18	−36.9
$C_6H_5-C_6H_4-NH_2$	PNBC	0.533 ± 0.010	1.11 ± 0.02	5600	3.85	−42.8
	PC	0.0744 ± 0.0021	0.235 ± 0.003	8800	5.32	−36.2
$O_2N-C_6H_4-C_6H_4-NH_2$	PNBC	0.0505 ± 0.0011	0.118 ± 0.003	6500	3.46	−44.7
	PC	0.00548 ± 0.00018	0.0205 ± 0.0009	10000	5.15	−37.1
$C_6H_5-NH_2$	PNBC	0.580 ± 0.018	—	—	—	—
	PC	0.120 ± 0.002	0.394 ± 0.005	9100	5.75	−34.3

* The terms have the same dimensions as in Tables 1—4.
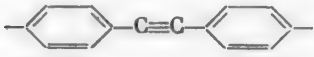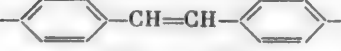
** PNBC is p-nitrobenzoyl chloride, and PC is picryl chloride.

ductance shown by the molecular systems discussed here with respect to the electronic interaction of 4,4'-substituents. In Table 6 we have given the values of f, which show that in the tolan system, the same as in the analogous stilbene system, the influence of the nitro group on the reactivity of the amino group is expressed more weakly than in the case of the biphenyl system. It is interesting that the tolan system, showing a higher unsaturation of the bonds in the bridge, is apparently even a somewhat poorer conductor of electronic effects than the stilbene system. If the geometric configuration of the tolan system is compared with that of stilbene and biphenyl, then in contrast to stilbene, which has a trans-configuration [11], and in contrast to biphenyl, where the hydrogen atoms in the 2,2'-positions create a hindrance to the internal rotation of the benzene rings around the single bond linking them (which determines the noncoplanar arrangement of these rings in biphenyl and its derivatives [12—14] in solutions or in the vapor state), the tolan system, due to its linearity and the considerable distance between its 2,2' hydrogen atoms (see [11], p. 404), differs from the other two systems discussed in that it shows the least steric hindrance for the electronic interaction of 4,4'-substituents. And if such interaction is still expressed more weakly in it than in the biphenyl and stilbene systems, then it should first be regarded as due to the fact that the acetylene bridge, inserted between two benzene rings, offers substantial resistance to the transmission of the mutual effect of substituents through it, while on the other hand, another explanation is that probably the carbon-carbon triple bond in organic molecules, despite its greater unsaturation and shorter length when compared with the C=C double bond, not only does not show a superior conductance of the electronic effects of groups attached to it, but is even somewhat inferior to the double bond in this respect. This conclusion is found to be in harmony with the comparative data obtained for the absorption spectra of diphenyl drivatives of polyynes and polyenes, where the conclusion was made that the first class of compounds show less complete conjugation than the second class [15] (see [1, 9]).

Regarding the energy parameters of the reactions studied in this paper, it can be said that the indicated reactions go at low values of E and ΔS^*, in which connection the reactions involving picryl chloride are characterized by having somewhat higher values for these terms than in the case of p-nitrobenzoyl chloride. It should also be mentioned that when different amines are reacted with the same electrophilic reagent, the changes in ΔS^* are, in general, considerably smaller than the changes in E when going from one amino derivative to another.

TABLE 6

Values of Factors f for the Molecular Systems of Tolan, Stilbene and Biphenyl

System	f_{25} for reaction with p-nitrobenzoyl chloride	f_{25} for reaction with picryl chloride
—◯—C≡C—◯—	4.06	4.65
—◯—CH=CH—◯—	4.89	5.12
—◯—◯—	10.6	13.6

SUMMARY

1. Based on a study of the kinetics of reaction of 4-aminotolan and 4-amino-4'-nitrotolan with p-nitrobenzoyl chloride and picryl chloride in benzene solution, and a comparison of the obtained results with the kinetics data for earlier investigated monotypic reactions involving amino and aminonitro derivatives of biphenyl and trans-stilbene, it was shown that the molecular system of tolan, in which the benzene rings are separated by an acetylenic bridge, is a poorer conductor of the mutual electronic effects of 4,4'-substituents than the biphenyl system, where the benzene rings are directly attached to each other.

2. The molecular system of tolan is a somewhat poorer conductor of the mutual electronic effects of 4,4'-substituents than the analogous trans-stilbene system, although the difference between the two systems in this respect is small.

LITERATURE CITED

[1] L. M. Litvinenko and N. F. Levchenko, Zhur. Obshchei Khim. 29, 924 (1959). [*]

[2] L. M. Litvinenko and A. P. Grekov, Ukrain. Khim. Zhur. 20, 194 (1954).

[3] L. M. Litvinenko, N. F. Levchenko, and A. N. Androsov, Zhur. Obshchei Khim. 28, 2046 (1958). [*]

[4] S. Ross and I. Kuntz, J. Am. Chem. Soc. 76, 3000 (1954).

[5] V. A. Izmail'skii, Collection; "Problems of aniline dye chemistry", [in Russian] (Transactions of 8th Conference on Aniline Dye Chemistry and Practice, Izd. AN SSSR, 1950), p. 88.

[6] V. A. Izmail'skii, G. V. Alekseeva and R. S. Tsekhanskii, Collection: "Some problems in the synthesis and application of dyes " (from the reports of the Scientific-Technical Conference on Problems Relating to the Synthesis and Application of Dyes) [in Russian] (Leningrad, Goskhimizdat, 1956), p. 76.

[7] L. M. Litvinenko and A. P. Grekov, Collection: Problems of Chemical Kinetics, Catalysis and Reactivity [in Russian] (Izd. AN SSSR, 1955), p. 860; Uchenye Zapiski Kharkov Univ. 71, Trudy Nauch.-Issledovatel. Inst. Khim. i Khim. Fakul'tet 14, 165 (1956).

[8] L. M. Litvinenko, A. P. Grekov, and S. V. Tsukerman, Ukrain. Khim. Zhur. 21, 510 (1955).

[9] L. M. Litvinenko, R. S. Cheshko, and A. D. Gofman, Zhur. Obshchei Khim. 27, 758 (1957). [*]

[10] L. M. Litvinenko, L. G. Syrovatka, T. S. Skoropisova, and S. V. Ostrovskaya, Ukrain. Khim. Zhur. 25, 189 (1959).

[11] A. I. Kitaigorodskii, Organic Crystal Chemistry [in Russian] (Izd. AN SSSR, 1955), p. 401.

[12] S. Samoilov and M. Dyatkina, Zhur. Fiz. Khim. 22, 1294 (1948).

[13] I. Karle and L. Brockway, J. Am. Chem. Soc. 66, 1974 (1944).

[14] O. Bastiansen, Acta Chem. Scand. 3, 408 (1949); C. A. 44, 6212a (1950); 44, 926 (1950; C. A. 45, 4105h (1951); O. Bastiansen and L. Smedvik, 8, 1593 (1954); C. A. 49, 9999i (1955).

[15] A. E. Gillam and E. S. Stern, Electronic Spectra of Organic Compounds [Russian translation] (IL, 1957), p. 119.

___

[*]Original Russian pagination. See C. B. Translation.

p-DI(2-CHLOROETHYL)AMINOPHENYLALANINE ("SARCOLYSIN")
AND ITS DERIVATIVES
III. α-N-ACYL DERIVATIVES*

E. N. Shkodinskaya, M. N. Vasil'eva, O. S. Vasina, and A. Ya. Berlin

The synthesis of p-di(2-chloroethyl)aminophenylalanine ("sarcolysin")$(ClCH_2CH_2)_2NC_6H_4CH_2CH(NH_2)COOH$ was reported by us earlier [1]. The HCl salt possesses highly valuable antitumor properties and is quite effective in the treatment of certain human malignant tumors [2, 3]. This was the first evidence in support of the theory that the activity of β-chloroethylamines is enhanced if they are coupled to compounds with metabolic activity [4].

It is quite possible for various sarcolysin derivatives, possessing somewhat different chemical and physico-chemical properties than sarcolysin itself, to show also a different antitumor effect, meaning by this a change both in the relative toxicity of a compound and in the specific direction of its action against certain types of malignant growths.

Starting from these considerations, we undertook a systematic synthesis of sarcolysin derivatives in which both the carboxyl group and the α-amino group were substituted [5].

In this paper we describe some α-N-acyl derivatives of p-di(2-chloroethyl)aminophenylalanine.

It is known that the N-formyl derivatives of many amino acids are easily formed by heating the amino acid with formic acid at 100°. However, it proved that the reaction of sarcolysin with anhydrous formic acid either does not go at all, or it goes with great difficulty and gives the desired compound in low yield. For this reason, we ran the formylation of sarcolysin in the presence of acetic anhydride [6], and this led to an 81% yield of α-N-formyl-sarcolysin.

In a similar manner, the refluxing of sarcolysin with acetic acid and acetic anhydride gave α-N-acetyl-sarcolysin in 80% yield.

It is indicated in the literature that amino acids having an iodoacetyl radical on the nitrogen possess the ability to inhibit tumor growth. Thus, N-iodoacetyltryptophan, N-iodoacetylleucine and N-iodoacetylphenyl-alanine respectively inhibit the growth of mouse sarcoma 37 to the extent of 42, 47,and 81% [7].

This observation caused us to synthesize also some α-N-haloacetyl derivatives of sarcolysin. Our first attempts to prepare N-chloroacetylsarcolysin, starting with sarcolysin and chloroacetic acid in the presence of acetic anhydride, led to obtaining a bright yellow compound with m.p. 146—149°, apparently being 2-methyl-4-[p-di(2-chloroethyl) aminobenzylidene]-2-oxazolin-5-one [8].

$$p\text{-}(ClCH_2CH_2)_2NC_6H_4CH_2\underset{\underset{NH_2}{|}}{C}HCOOH + ClCH_2COOH \xrightarrow{(CH_3CO)_2O}$$

$$\rightarrow p\text{-}(ClCH_2CH_2)_2NC_6H_4CH=\underset{\underset{\underset{C-CH_3}{N\quad O}}{}}{C-CO}$$

---
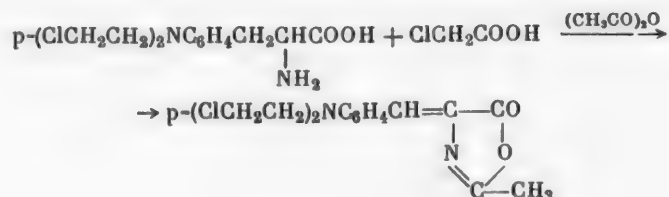
*For Communications I and II see [1] and [6], respectively.

Attempts to obtain the desired compound by reacting sarcolysin with chloroacetyl chloride, either under the conditions of long refluxing in ethyl acetate [9] or by heating in a sealed tube, also proved unsuccessful.

In view of the encountered difficulties, we turned to the elegant method [10] of forming both the amide and the peptide linkage from the corresponding acid and amine using dicyclohexylcarbodiimide.

$$RCOOH + H_2NR' + C_6H_{11}N=C=NC_6H_{11} \rightarrow RCONHR' + C_6H_{11}NHCONHC_6H_{11}$$

In this manner, starting with the isopropyl ester of sarcolysin, we readily obtained the isopropyl ester of α-N-chloroacetylsarcolysin and the isopropyl ester of α-N-iodoacetylsarcolysin.

We wish to thank the co-workers in the analytical laboratory, under the supervision of A. D. Chinaeva, for running the analyses.

EXPERIMENTAL

α-N-Formylsarcolysin. Into a three-necked flask, fitted with a stirrer, dropping funnel and reflux condenser, was charged 2 g of sarcolysin and 30 ml of 96% formic acid. The flask was heated to 50—60°, and then 8 ml of acetic anhydride was added dropwise in 20 min. The solution was then heated for another 30 min at 60°, after which it was cooled and treated with 110 ml of water. After cooling, the crystalline compound was filtered, washed with water, and dried in a vacuum desiccator over phosphorus pentoxide. We obtained 1.7 g (80.9%) of α-N-formyl-sarcolysin with m.p. 149—151°. After recrystallization from 96% alcohol, m.p. 151—152°.

Found %: C 50.75; H 5.65; N 8.55. $C_{14}H_{18}O_3N_2Cl_2$. Calculated %: C 50.46; H 5.44; N 8.4.

Using different conditions, and specifically after a double refluxing (3 hr each) of sarcolysin with 98% formic acid, with removal of the acid by vacuum distillation each time, we were able to isolate N-formylsarcolysin in a total yield of only 20%.

α-N-Acetylsarcolysin. With stirring and heating at a bath temperature of 60°, 30 ml of acetic anhydride was added dropwise in 10 min to a mixture of 6 g of sarcolysin and 60 ml of glacial acetic acid. The heating was continued for another 10 min. The light-yellow solution was poured into 200 ml of cold water, and then water was added until a precipitate began to form. The obtained substance was filtered, washed with water, and dried in a vacuum desiccator over phosphorus pentoxide. We obtained 5.3 g (76%) of α-N-acetylsarcolysin with m.p. 151—152°. M. p. 153—154° (from alcohol).

Found %: C 51.84; H 5.73; N 8.13; Cl 20.73. $C_{15}H_{20}O_3N_2NCl_2$. Calculated %: C 51.89; H 5.76; N 8.07; Cl 20.43.

2-Methyl-4-[p-di(2-chloroethyl)aminobenzylidene]-2-oxazolin-5-one. To 15 g of monochloroacetic acid were added 1 ml of acetic anhydride and 1 g of sarcolysin, after which the reaction mixture was stirred for 15 min at 70°. The bright yellow viscous solution was poured into water (about 700 ml). The obtained oil was washed with water and then extracted with ether. The ether solution was dried, and the ether was removed in vacuo to give a bright yellow crystalline compound, difficultly soluble in ether. Weight 0.5 g, m.p. 146—149°.

Found %: N 8.92; Cl 21.89. $C_{15}H_{16}O_2N_2Cl_2$. Calculated %: N 8.56; Cl 21.67.

Isopropyl ester of α-N-iodoacetylsarcolysin. A charge of 1.73 g of the isopropyl ester of sarcolysin, obtained from the hydrochloride [5], and 10 ml of dry chloroform was placed in a 100-ml flask. The obtained solution was treated with a solution of 1.03 g of dicyclohexylcarbodiimide in chloroform (10 ml), followed by the addition of 0.93 g of iodoacetic acid (m.p. 80—83°) in chloroform. Both a heating-up of the reaction mixture to 35° and the separation of a white precipitate were observed during the addition of the iodoacetic solution. The mixture was shaken for 1 hr, and then allowed to stand overnight at room temperature. Removal of the dicyclohexylurea by filtration, and evaporation of the filtrate to dryness, left 2.9 g of liquid residue, which solidified when rubbed with anhydrous alcohol and ether. A crystalline compound with m.p. 104—108° was obtained after recrystallization from anhydrous alcohol. Yield 1.7 g (68%). M.p. 108—110° (from alcohol).

Found %: C 42.06; H 5.02, N 5.63. $C_{18}H_{25}O_3N_2Cl_2I$. Calculated %: C 41.95; H 4.91; N 5.43.

Isopropyl ester of α-N-chloroacetylsarcolysin. A solution of 0.47 g of freshly distilled chloroacetic acid in 10 ml of $CHCl_3$ was added to a solution of 1.73 g of the isopropyl ester of sarcolysin and 1.03 g of dicyclohexyl-

carbodiimide in 20 ml of dry chloroform. The reaction mixture was shaken for 1 hr, and then allowed to stand overnight at room temperature. The obtained precipitate of dicyclohexylurea was filtered, and the filtrate was evaporated in vacuo to dryness (bath temperature not above 50°). The residue was rubbed with ether, and the obtained product was filtered and dried. We obtained 1.05 g of compound with m.p. 85—89°. After 3 recrystallizations from anhydrous alcohol, m.p. 89—92°.

Found %: C 50.84; H 5.95; N 6.79. $C_{18}H_{25}O_3N_2Cl_3$. Calculated %: C 51.01; H 5.94; N 6.61.

SUMMARY

The preparation of the following α-N-acyl derivatives of p-di(2-chloroethyl)amino-DL-phenylalanine (sarcolysin) is described: α-N-formylsarcolysin, α-N-acetylsarcolysin, isopropyl ester of α-N-iodoacetylsarcolysin, and isopropyl ester of α-N-chloroacetylsarcolysin. 2-Methyl-4-[p-di(2-chloroethyl)aminobenzylidene]-2-oxazolin-5-one was also obtained.

LITERATURE CITED

[1] L. F. Larionov, A. S. Khokhlov, E. N. Shkodinskaya, O. S. Vasina and V. I. Trusheikina, a) Soviet Author's Certificate No. 104, 781, July 5, 1954; b) Byull. Éksp. Biol. Med. 39, 48 (1955); c) Lancet 23, 169 (1955).

[2] V. I. Trusheikina, Voprosy Onkol. 2, 222 (1956).

[3] N. N. Blokhin, Tenth Session of Academy of Medical Sciences of the USSR, Themes of Papers [in Russian] (1956); Voprosy Onkol 3, 323 (1956).

[4] L. F. Larionov, Themes of Papers Delivered at 8th All-Union Convention of Physiology, Biochemistry and Pharmacology [in Russian] (1955) p. 375.

[5] N. A. Vodolazskaya, M. A. Novikova, E. N. Shkodinskaya, O. S. Vasina, A. Ya. Berlin, and L. F. Larionov, Byull. Éksp. Biol. Med. No. 11, 76 (1957). *

[6] Brit. Patent 585,413; C. A. 41, 4175a (1947).

[7] O. Friedman and A. Rutenberg, Proc. Soc. Exptl. Biol. Med. 74, 764 (1950).

[8] See M. Bergmann and F. Stern, Ann. 448, 20 (1926).

[9] E. Ronwin, J. Org. Chem. 18, 127 (1953); 18, 1546 (1953).

[10] J. Sheehan and G. Hess, J. Am. Chem. Soc. 77, 1067 (1955).

*Original Russian pagination. See C. B. Translation.

CATALYTIC CONDENSATION OF SCHIFF BASES WITH ORGANIC COMPOUNDS.

CONDENSATION OF SCHIFF BASES WITH ACETALDEHYDE

N. S. Kozlov and I. A. Shur

Perm Agricultural Institute

The synthesis of 2-phenyl-5,6-benzoquinolone and its derivatives has received very little study. At the present time the principal method for obtaining the compound is the Doebner method [1], based on the condensation of 2-naphthylamine and aromatic aldehydes with pyrotartaric acid. The compound obtained first in this reaction is 2-phenyl-5,6-benzoquinoline-4-carboxylic acid or its derivatives, which by decarboxylation is converted to 2-phenyl-5,6-benzoquinoline or its derivatives. Individual methods for obtaining 2-phenyl-5,6-benzoquinoline are described in the paper by John and Noziczka [2], where the condensation of 2-naphthylamine with benzalacetone is described, leading to the synthesis of 4-methyl-2-phenyl-5,6-benzoquinoline, and also in the paper by Kalff [3], who synthesized 2-phenyl-5,6-benzoquinoline from 2-naphthylamine and phenylpropargylaldehyde. A new method for the synthesis of 2-phenyl-5,6-benzoquinolone and its various derivatives [5], based on the joint catalytic condensation of 2-naphthylamine and aromatic aldehydes with acetylene, was described in a paper by one of us [4]. Based on the concepts regarding the mechanism of the last named reaction, we expressed the theory that the corresponding Schiff base shows catalytic condensation with the monoethylideneaniline formed in the reaction process, since the latter, having labile hydrogen atoms, adds to the azomethine group. We consider the mono-ethylidene base as a chemical analog of acetaldehyde [6]; in this connection it was assumed that the condensation of a Schiff base with acetaldehyde is possible. That such a reaction is possible is also supported by the data obtained by one of us [7], where the condensation of benzalaniline with acetaldehyde to yield 2-phenylquinoline was accomplished, but the yield of the latter was extremely small.

In this paper we studied the condensation of Schiff bases, obtained from 2-naphthylamine and various aromatic aldehydes, with acetaldehyde. The following Schiff bases were taken for reaction with acetaldehyde: benzal-2-naphthylamine, m- and p-nitrobenzal-2-naphthylamine, 2-hydroxybenzal-2-naphthylamine, 4-methoxybenzal-2-naphthylamine, 4-dimethylaminobenzal-2-naphthylamine, and piperonal-2-naphthylamine. As the end reaction products we obtained 2-phenyl-5,6-benzoquinoline and its nitro-, hydroxy-, methoxy-, dimethylamino-, and methylenedioxy- derivatives.

The mechanism of the reaction studied by us can be depicted as follows.
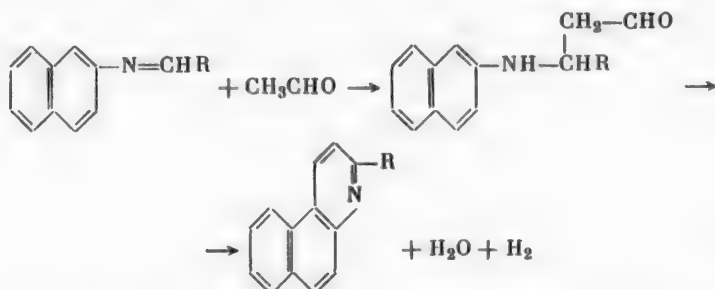
where R = C_6H_5, o-HOC_6H_4, m- and p-$NO_2C_6H_4$, p-$CH_3OC_6H_4$, p-$(CH_3)_2NC_6H_4$, $CH_2O_2C_6H_3$

Free hydrogen is not liberated here; apparently a part of the Schiff base is consumed for the hydrogenation, which is in agreement with the literature data [8]. The reaction studied by us has a catalytic character. As catalyst we used 2-naphthylamine hydrochloride. We had previously used 2-naphthylamine hydrochloride as an active catalyst in the condensation of Schiff bases with ketones [9]. There is no doubt but that other aldehydes besides acetaldehyde can be reacted with Schiff bases; this opens up a new path for the synthesis of many derivatives of 2-phenyl-5,6-benzoquinoline.

EXPERIMENTAL

The method of study was essentially as follows. To a well-mixed mixture of 0.01 g-mole (2.5—3.0 g) of Schiff base, 0.5 g of 2-naphthylamine hydrochloride and 10 ml of alcohol in a test tube was added 0.015 g-mole (0.60 g) of acetaldehyde with cooling. Then the test tube was sealed and heated in a boiling water bath for 1—3 hr, after which it was cooled. The crystalline product was treated with dilute alcoholic ammonia solution, and then recrystallized from pyridine. The obtained results are given in the table.

Expt. No.	Name of synthesized compound	Empirical formula	Yield (%)	Our melting point	Literature data [4, 5]
1	2-Phenyl-5,6-benzoquinoline	$C_{19}H_{13}N$	43.3	188°	188°
2	2-(2-Hydroxyphenyl)-5,6-benzo-quinoline	$C_{19}H_{13}ON$	50.0	218	218
3	2-(4-Methoxyphenyl)-5,6-benzo-quinoline	$C_{20}H_{15}ON$	21.1	191—192	192
4	2-(3-Nitrophenyl)-5,6-benzoquino-line	$C_{19}H_{12}O_2N_2$	40.0	183	182—183
5	2-(4-Nitrophenyl)-5,6-benzoquino-line	$C_{19}H_{12}O_2N_2$	24.1	196	196
6	2-(4-Dimethylaminophenyl)-5,6-benzoquinoline	$C_{21}H_{18}N_2$	10.2	242—243	237—238
7	2-Piperonyl-5,6-benzoquinoline	$C_{20}H_{13}O_2N$	10.2	182—183	179

From the data given in the table it follows that if the reaction is run under constant conditions, the structure of the Schiff base exerts an effect on the yield of the quinoline base. The low yield of the base in the synthesis of 2-(4-dimethylaminophenyl)-5,6-benzoquinoline and 2-piperonyl-5,6-benzoquinoline is due to the large formation of tarry products. In the synthesis of 2-(4-methoxyphenyl)-5,6-benzoquinoline, together with the main product, substantial amounts of a substance with m.p. 260° were obtained, which substance is being studied at the present time. The melting points of the compounds obtained by us coincide with those given in the literature [4, 5]. The mixed melting points of our compounds with authentic specimens were not depressed.

SUMMARY

A new method has been developed for the synthesis of 2-phenyl-5, 6-benzoquinoline and its various derivatives. The method is based on the catalytic condensation of the Schiff bases represented by benzal-2-naphthyl-amine and its derivatives with acetaldehyde. Seven compounds in this series were synthesized by this procedure.

LITERATURE CITED

[1] O. Doebner, Ber. 27, 352 (1894).

[2] H. John and Fr. Noziczka, J. prakt. Chem. 111, 65 (1925).

[3] J. Kalff, Rec. trav. chim. 46, 594 (1927).

[4] N. S. Kozlov and O. K. Koz'minykh, Zhur. Obshchei Khim. 27, 1628, 3122 (1957).*

[5] N. S. Kozlov and O. K. Koz'minykh, Doklady Akad. Nauk SSSR 114, 785 (1957).*

*Original Russian pagination. See C. B. Translation.

[6] N. S. Kozlov, Zapiski Akad. Nauk Beloruss. SSSR <u>5</u>, 149 (1936).

[7] N. S. Kozlov, Zhur. Obshchei Khim. <u>8</u>, 413 (1938).

[8] R. C. Elderfield, Heterocyclic Compounds [Russian translation] Vol. <u>4</u>, (1938) p. 477.

[9] N. S. Kozlov and I. A. Shur, Zhur. Obshchei Khim. <u>29</u>, 2706 (1959).[*]

---

[*]Original Russian pagination. See C. B. Translation.

THIOCARBANILIDE DERIVATIVES

II. SYNTHESIS OF ETHOXY- AND CARBOXY-SUBSTITUTED
UNSYMMETRICAL THIOCARBANILIDE DERIVATIVES

R. G. Dubenko and P. S. Pel'kis

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR

In the previous paper [1] we described some sulfonamido- and carboxy-substituted symmetrical thiocarbanilide derivatives. It is indicated in the literature that the introduction of alkoxy groups into the phenyl rings of thiocarbanilide leads to compounds with substantial antibacterial activity [2], in particular, antitubercular activity [3]. For this reason it seemed of interest to prepare a number of ethoxy- and carboxy-substituted unsymmetrical thiocarbanilide derivatives. These derivatives were obtained from the corresponding substituted phenyl isothiocyanates and amines by the scheme

$$RNCS + R'NH_2 \longrightarrow RNHCNHR'.$$
$$\underset{S}{\|}$$
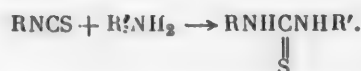
The substituted phenyl isothiocyanate derivatives needed for the syntheses were prepared from the corresponding substituted aniline derivatives and thiophosgene in dilute hydrochloric acid medium [4]. This procedure gives the aryl isothiocyanates in good yields. The compounds synthesized by us are given in the table. They were obtained either as white or pale yellow crystalline compounds with sharp melting points. The compounds are slightly soluble in organic solvents, and are readily soluble in dilute alkali solutions.

The ultraviolet absorption curves of some of the substituted unsymmetrical thiocarbanilide derivatives are shown in Fig. 1 and 2.

A SF-4 spectrophotometer was used to make the measurements in alcohol solution.

EXPERIMENTAL

1-(p-ethoxy)-3-(p-sulfamoyl)-thiocarbanilide (I). A mixture of 2 g of p-ethoxyphenyl isothiocyanate and 2 g of p-aminobenzenesulfonamide (white streptocide) in 50 ml of acetone was heated under reflux on the water bath for 5 hr. A part of the acetone was removed in vacuo. On cooling, the thiocarbanilide separated as pale - yellow crystals. The precipitate was filtered, washed in sequence with alcohol and ether, dried in vacuo, and recrystallized from alcohol.

1-(p-Ethoxy)-3-(p-acetamidosulfonyl)-thiocarbanilide (II). From 3 g of p-ethoxyphenyl isothiocyanate and 3.9 g of sulfanilylacetamide (albucid) we obtained 6 g (91%) of 1-(p-ethoxy)-3-(p-acetamidosulfonyl)-thiocarbanilide. Recrystallization from alcohol gave the compound as pale-yellow crystals.

1-(p-Ethoxy)-3-[p-(4-sulfamoylanilino)sulfonyl]-thiocarbanilide (III). For reaction we took 2 g of p-ethoxyphenyl isothiocyanate and 3.7 g of 4'-sulfamoylsulfanilanilide (disulfan). Recrystallization from alcohol gave the thiocarbanilide as a pale-yellow crystalline powder.

1-(p-Ethoxy)-3-(p-cyanoaminosulfonyl)-thiocarbanilide (IV). For reaction we took 3 g of p-ethoxyphenyl isothiocyanate and 3.3 g of sulfanilylcyanamide (sulcimide). Recrystallization from acetone gave the thiocarbanilide as a yellow crystalline product.
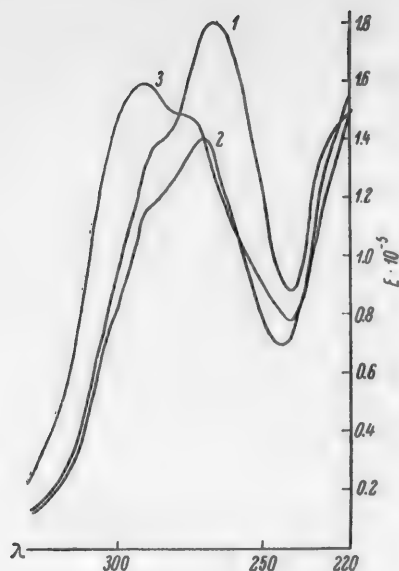
Fig. 1. Absorption curves of un-
symmetrical thiocarbanilide deriva-
tives in alcohol.

1) 1-(p-Ethoxy)-3-(p-sulfamoyl)-
thiocarbanilide (I); 2) 1-(p-ethoxy)-
-3-[p-(4,6-dimethyl-2-pyrimidinyl)
aminosulfonyl]-thiocarbanilide (V);
3) 1-(p-ethoxy)-3-[p-(5-ethyl-1,3,4-
thiadiazol-2-yl)aminosulfonyl]-thio-
carbanilide (VII).
Concentration of solutions: (I) and (V)
2.2×10^{-5}M; (VII) 1.65×10^{-5}M.
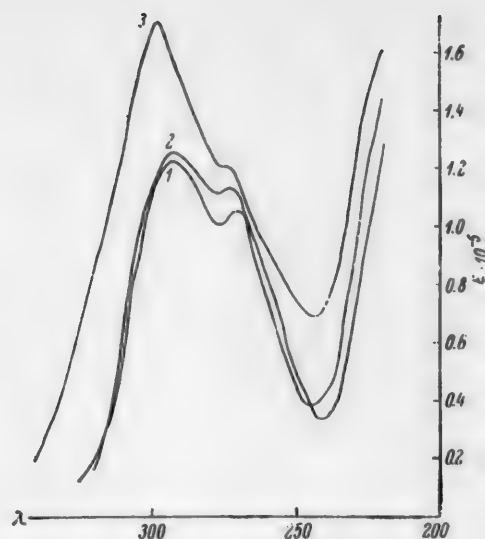
Fig. 2. Absorption curves of unsymmetrical thio-
carbanilide derivatives in alcohol.

1) 1-(p-Carboxy)-3-(p-sulfamoyl)-thiocarbanilide
(X); 2) 1-(p-carboxy)-3-[p-(4,6-dimethyl-2-
pyrimidinyl)aminosulfonyl]-thiocarbanilide (XI);
3) 1-(p-carboxy)-3-[p-(5-ethyl-1,3,4-thiadiazol-
2-yl)aminosulfonyl]-thiocarbanilide (XV).

Concentration of solutions: (X) and (XI) $2.2 \times$
10^{-5}M; (XV) 1.65×10^{-5}M.

1-(p-Ethoxy)-3-[p-(4,6-dimethyl-2-pyrimidinyl)aminosulfonyl]-thiocarbanilide (V). For reaction we took
2 g of p-ethoxyphenyl isothiocyanate and 3.1 g of 2-sulfanilamido-4,6-dimethylpyrimidine (sulfamethazine). The
obtained product was recrystallized from alcohol.

1-(p-Ethoxy)-3-[p-(2-thiazolyl)aminosulfonyl]-thiocarbanilide (VI). From 2 g of p-ethoxyphenyl isothio-
cyanate and 2.7 g of N^1-2-thiazolylsulfanilamide (sulfathiazole) we obtained 4.4 g of the thiocarbanilide. The
compound was recrystallized from alcohol.

1-(p-Ethoxy)-3-[p-(5-ethyl-1,3,4-thiadiazol-2-yl)aminosulfonyl]-thiocarbanilide (VII). For reaction we
took 3 g of p-ethoxyphenyl isothiocyanate and 4.7 g of N^1-(5-ethyl-1,3,4-thiadiazol-2-yl)sulfanilamide (ethazole).
After recrystallization from alcohol we obtained 6.6 g of the thiocarbanilide.
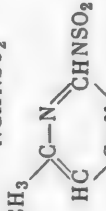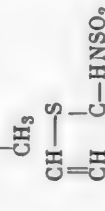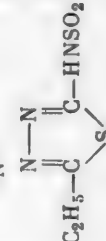
1-(p-Ethoxy)-3-(p-carbethoxy)-thiocarbanilide (VIII). For reaction we took 2 g of p-ethoxyphenyl isothio-
cyanate and 1.6 g of p-carbethoxyaniline (anesthesine). The yield of the thiocarbanilide was 3.4 g.
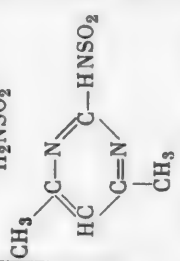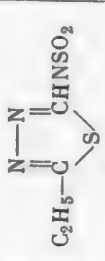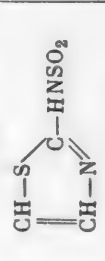
1-(p-Ethoxy)-3-(m-hydroxy-p-carboxy)-thiocarbanilide (IX). For reaction we took 2 g of p-ethoxyphenyl
isothiocyanate and 1.7 g of the sodium salt of p-aminosalicylic acid (PASA). The thiocarbanilide was obtained
as pale yellow crystals.

1-(p-Carboxy)-3-(p-sulfamoyl)-thiocarbanilide (X). From 2 g of p-carboxyphenyl isothiocyanate and 2.2 g
of p-aminobenzenesulfonamide (white streptocide) we obtained 3.9 g of 1-(p-carboxy)-3-(p-sulfamoyl)-thiocarbanil-
ide. The product was purified by precipitation from alkaline solution (5% aqueous NaOH solution) with 5% hydrochloric
acid.

Ethoxy- and Carboxy-Substituted Unsymmetrical Thiocarbanilides of General Formula

$$R\left\langle\ \right\rangle NH$$
$$R'\left\langle\ \right\rangle NH - C=S$$

Expt. no.	R	R'	Melting point	Yield (in %)	Empirical formula	% N		% S	
						found	calculated	found	calculated
(I)	C_2H_5O	H_2NSO_2	176°	94	$C_{15}H_{17}O_3N_3S_2$	11.93, 12.10	11.96	—	—
(II)	C_2H_5O	$CH_3COHNSO_2$	128	91	$C_{17}H_{19}O_4N_3S_2$	10.39, 10.47	10.69	—	—
(III)	C_2H_5O	$H_2NSO_2\langle\ \rangle HNSO_2$	174	88	$C_{21}H_{22}O_5N_4S_3$	10.86, 10.92	11.07		
(IV)	C_2H_5O	$NCHNSO_2$	177	95	$C_{16}H_{16}O_3N_4S_2$	14.91, 15.13	14.89		
(V)	C_2H_5O	(heterocyclic structure)	152	93	$C_{21}H_{23}O_3N_5S_2$	15.13, 15.04	15.32		
(VI)	C_2H_5O	(heterocyclic structure)	179	91	$C_{18}H_{18}O_3N_4S_3$	12.83, 12.54	12.90		
(VII)	C_2H_5O	(heterocyclic structure)	92	92	$C_{19}H_{21}O_3N_5S_3$	14.75, 14.84	15.11		
(VIII)	C_2H_5O	C_2H_5OOC	134	88	$C_{18}H_{20}O_3N_2S$	8.21, 8.37	8.14	9.06, 9.17	9.30

Expt. no.	R	R'	Melting point	Yield (in %)	Empirical formula	% N		% S	
						found	calculated	found	calculated
(IX)	C_2H_5O	m-OH, p-COONa	doesn't melt	Quantitative	$C_{18}H_{15}O_4N_2SNa$	8.13, 8.11	7.91	—	—
(X)	COOH	H_2NSO_2 (structure with CH_3, $C-N$, $C-HNSO_2$)	145°	99	$C_{14}H_{13}O_4N_3S_2$	11.96, 11.92	11.96	—	—
(XI)	COOH	(structure with CH_3)	172	94	$C_{20}H_{19}O_4N_5S_2$	15.05, 15.13	15.32	—	—
(XII)	COOH	H_2NSO_2 — $HNSO_2$ (structure)	137 doesn't melt	98	$C_{20}H_{18}O_6N_4S_3$	10.79, 10.85	11.07	—	—
(XIII)	COONa	SO_3Na	doesn't melt	95	$C_{14}H_{10}O_5N_2S_2Na_2$	7.02, 7.12	7.07	—	—
(XIV)	COOH	C_2H_5OOC	197	94	$C_{17}H_{16}O_4N_2S$	8.12, 8.19	8.14	9.04, 8.95	9.30
(XV)	COOH	C_2H_5-C (structure $N-N$, $CHNSO_2$, S)	177	82	$C_{18}H_{17}O_4N_5S_3$	—	—	20.36, 20.42	20.73
(XVI)	COOH	(structure $CH-S$, $C-HNSO_2$, $CH-N$)	143	98	$C_{17}H_{14}O_4N_4S_3$	12.58, 12.69	12.91	—	—
(XVII)	COOH	$H_2NCOHNSO_2$	159	81	$C_{15}H_{14}O_5N_4S_2$	—	—	15.91, 16.04	16.24
(XVIII)	COOH	CH_3CO	doesn't melt	73	$C_{16}H_{14}O_3N_2S$	8.55, 8.70	8.92	—	—

This thiocarbanilide was also obtained from mustard oil, white streptocide and p-aminobenzoic acid. The mixed melting point of the two preparations was not depressed.

The thiocarbanilide derivatives described below were purified by precipitation from dilute alkali solution with dilute hydrochloric acid.

1-(p-Carboxy)-3-[p-(4,6-dimethyl-2-pyrimidinyl)aminosulfonyl]-thiocarbanilide (XI). From 2.4 g of para-carboxyphenyl isothiocyanate and 3.4 g of 2-sulfanilamido-4,6-dimethylpyrimidine (sulfamethzaine) we obtained 5.4 g of the thiocarbanilide.

1-(p-Carboxy)-3-[p-(4-sulfamoylanilino)sulfonyl]-thiocarbanilide (XII). For reaction we took 2 g of p-carboxy-phenyl isothiocyanate and 3.8 g of 4'-sulfamoylsulfanilanilide (disulfan). The thiocarbanilide was obtained as a white crystalline powder.

1-(p-Carboxy)-3-(p-sulfo)-thiocarbanilide (XIII). From 2 g of p-carboxyphenyl isothiocyanate, 2 g of sulfanilic acid and 1.3 g of sodium carbonate we obtained 4.1 g of the disodium salt of the thiocarbanilide. The product does not melt.

1-(p-Carboxy)-3-(p-carbethoxy)-thiocarbanilide (XIV). For reaction we took 2 g of p-carboxyphenyl isothio-cyanate and 1.6 g of p-carbethoxyaniline (anesthesine). A white crystalline product was obtained.

1-(p-Carboxy)-3-[p-(5-ethyl-1,3,4-thiadiazol-2-yl)aminosulfonyl]-thiocarbanilide (XV). The thiocarbanilide, prepared from 3 g of p-carboxyphenyl isothiocyanate and 4.8 g of N^1-(5-ethyl-1,3,4-thiadiazol-2-yl)-sulfanilamide (ethazole), was obtained as white crystals after precipitation from 5% aqueous NaOH solution with dilute hydrochloric acid.

1-(p-Carboxy)-3-[p-(2-thiazolyl)aminosulfonyl]-thiocarbanilide (XVI). For reaction we took 2.5 g of p-carboxyphenyl isothiocyanate and 3.5 g of N^1-2-thiazolylsulfanilamide (sulfathiazole). The compound was obtained as white crystals.

1-(p-Carboxy)-3-(p-ureidosulfonyl)-thiocarbanilide (XVII). For reaction we took 2 g of p-carboxyphenyl isothiocyanate and 2 g of sulfanilylurea (urosulfan). The compound was obtained as white crystals.

1-(p-Carboxy)-3-(p-acetyl)-thiocarbanilide (XVIII). For reaction we took 2.68 g of p-carboxyphenyl iso-thiocyanate and 2 g of p-aminoacetophenone. The thiocarbanilide was obtained as yellow crystals.

SUMMARY

Eighteen new substituted thiocarbanilide derivatives were synthesized. Their ultraviolet absorption spectra were measured.

LITERATURE CITED

[1] R. G. Dubenko and P. S. Pel'kis, Zhur. Obshchei Khim. 29, 885 (1959).*

[2] C. F. Huebner, J. L. Marsh, R. H. Mizzoni, R. P. Mull, D. C. Schroeder, H. A. Troxell, and C. R. Scholz, J. Am. Chem. Soc. 75, 2274 (1952).

[3] E. A. Konopka, P. C. Eisman, R. L. Mayer, F. Parker, Jr., and S. L. Robbins, Am. Rev. Tuberc. 70, 130 (1954); L. Doub, L. Richardson, and others, J. Am. Chem. Soc. 80, 2205 (1958).

[4] R. L. McKee and R. W. Bost, J. Am. Chem. Soc. 68, 2506 (1946).

Received October 6, 1958

*Original Russian pagination. See C. B. Translation.

TRIHALOMETHYLATION OF ORGANIC COMPOUNDS

N. N. Yarovenko and A. S. Vasil'eva

The purpose of this work was to find ways of replacing the labile hydrogen atom in various compounds by the trihalomethyl group. This problem had been solved by us earlier for organic compounds containing the hydroxyl group [1].

In this paper we established that with a similar procedure it is possible to obtain thioethers from thioalcohols, and tertiary amines from secondary amines, where the products have the trichloromethyl group present on sulfur or on nitrogen, respectively. The reaction goes in two stages: The first is introduction of the halothiocarbonyl group into the organic molecule, and the second is replacement of the sulfur in the thiocarbonyl group by chlorine. As is known, it has proved impossible to obtain these compounds by other procedures [2].

Compounds having the fluorodichloromethyl group on the heteroatom can be obtained in a similar manner by the chlorination of the esters and thioesters of fluorothiocarbonic acid.

Tertiary amines containing the trichloromethyl group on nitrogen are hydrolyzed with extreme ease to the dialkylamides of chlorocarbonic acid.

$$RSH \xrightarrow{CSCl_2} RSC\begin{smallmatrix}S\\ \diagdown Cl\end{smallmatrix} \xrightarrow{Cl_2} RSCCl_3$$

$$R_2NH \xrightarrow{CSCl_2} R_2NC\begin{smallmatrix}S\\ \diagdown Cl\end{smallmatrix} \xrightarrow{Cl_2} R_2NCCl_3 \quad R=CH_2Cl-CH_2-$$
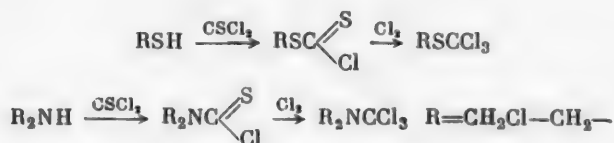
EXPERIMENTAL

β-Chloroethyl ester of dithiofluorocarbonic acid. Into a glass flask, fitted with an outlet tube and connected to a wash bottle containing sulfuric acid, was charged 8 g of thiocarbonyl chloride fluoride [3], and then with cooling in liquid air, 7 g of β-chloroethyl mercaptan was added. Then with stirring, the reaction mixture was warmed up slowly to 0°, kept at this temperature for 2—3 hr, and allowed to stand overnight at room temperature. The next day the reaction mixture was distilled under reduced pressure, washed with water, dried over sodium sulfate, and redistilled. Yield 2.5 g (20.2%). The compound was obtained as a pale-yellow liquid with a mustard odor. It is readily soluble in the common organic solvents.

B. p. 72° (16 mm), n_D^{17} 1.5731, d_4^{17} 1.4731.
Found %: C 23.15; H 2.71; F 11.94; Cl 22.8. $C_3H_4S_2FCl$. Calculated %: C 22.71; H 2.53; F 11.98; Cl 22.40.

Fluorodichloromethyl β-chloroethyl sulfide. Four grams of the β-chloroethyl ester of dithiofluorocarbonic acid was saturated with chlorine at about 40°. When the weight increase due to chlorine was 3.5 g, the reaction mixture was washed with water, dried over sodium sulfate, and distilled. Yield 1.7 g (34%).

B. p. 80° (18 mm), n_D^{16} 1.5349, d_4^{16} 1.5801.
Found %: S 16.46; F 9.18; Cl 54.05. $C_3H_4SFCl_3$. Calculated %: S 16.20; F 9.61; Cl 53.80.

Trichloromethyl β-chloroethyl sulfide. In a similar manner as the above, from 8.75 g of the β-chloroethyl ester of dithiochlorocarbonic acid, we obtained 3.2 g (15%) of the indicated sulfide, b.p. 97—105° (18 mm), n_D^{15} 1.5490, d_4^{15} 1.6590.

<u>Trichloromethyldiethylamine.</u> A solution of 5 g of the diethylamide of chlorothiocarbonic acid in 10 ml of chloroform was saturated with chlorine, maintaining the temperature of the reaction mixture not greater than 35-40°, by cooling. Then, when the evolution of heat had ceased, the sulfur dichloride and chloroform were distilled under reduced pressure. The solid residue was dissolved in chloroform, and again the solvent and liquid reaction products were removed by distillation under reduced pressure. The residue in the flask weighed about 5 g (76%). The compound was obtained as a white solid. It decomposes when heated, and reacts very vigorously with water.

Found %: N 7.21; Cl 56.35. $C_5H_{10}NCl_3$. Calculated %: N 7.35; Cl 55.80.

Hydrolysis with the calculated amount of water yields the diethylamide of chlorocarbonic acid.

<u>Fluorodichloromethyl phenyl ether.</u> Here 2.5 g of the phenyl ester of fluorothiocarbonic acid [3] was saturated with chlorine at 40−45° until the weight increase due to chlorine was 4.5 g. Then the sulfur chlorides were distilled off. The residue distilled at 84° (24 mm). Yield 5.2 g (80%).

B.p. 84° (24 mm), n_D^{15} 1.4971, d_4^{15} 1.3220.
Found %: C 42.10; H 2.70; F 10.24; Cl 36.40. $C_7H_5OFCl_2$. Calculated %: C 42.05; H 2.50; F 9.74; Cl 36.3.

SUMMARY

A method was described for replacing the labile hydrogen atom in alcohols, mercaptans and secondary amines by the trihalomethyl group.

LITERATURE CITED

[1] N. N. Yarovenko and A. S. Vasil'eva, Zhur. Obshchei Khim. <u>28</u>, 2502 (1958).*

[2] I. B. Douglass, F. T. Martin, and R. Addor, J. Org. Chem. <u>16</u>, 1297 (1951).

[3] N. N. Yarovenko and A. S. Vasil eva, Zhur. Obshchei Khim. <u>29</u>, 3792 (1959).*

---

*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF COMPOUNDS WITH TRIFLUOROMETHYL GROUP ON SULFUR

N. N. Yarovenko and A. S. Vasil'eva

Only two methods for the preparation of trifluoromethylsulfenyl chloride are known at the present time: by the chlorination of either hexafluorodimethyl disulfide or bis(trifluoromethylthio)mercury [1]. The fluorination of trichloromethylsulfenyl chloride fails to yield trifluoromethylsulfenyl chloride. We established that difluorochloromethylsulfenyl chloride, in contrast to trichloromethylsulfenyl chloride, is capable of reacting with antimony trifluoride in the presence of antimony pentachloride with a partial retention of the C—S bond. In a similar manner, we were able to obtain trifluoromethylsulfenyl bromide by the fluorination of difluorobromomethylsulfenyl bromide, and trifluoromethyl β-chloroethyl sulfide by the fluorination of difluorochloromethyl β-chloroethyl sulfide.

$$CF_2XSX \xrightarrow{SbF_3 + SbCl_5} CF_3SX \quad (X = Cl, Br)$$

$$CF_2ClSCH_2CH_2Cl \xrightarrow{SbF_3 + SbCl_5} CF_3SCH_2CH_2Cl$$
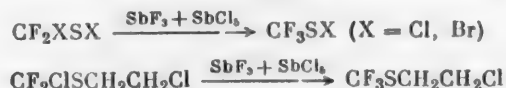
To make these reactions go it is necessary to use a large excess of antimony trichloride and a comparatively small amount of antimony pentachloride, and especially important here is a prior thorough mixing of the fluorinating agents [2]. We obtained the previously unknown difluorochloromethyl β-chloroethyl sulfide by the addition of difluorochloromethylsulfenyl chloride to ethylene.

$$CF_2ClSCl \xrightarrow{CH_2=CH_2} S\begin{cases} CF_2Cl \\ CH_2CH_2Cl \end{cases}$$
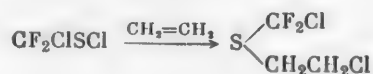
This reaction goes very easily at room temperature and atmospheric pressure. As is known, in contrast to difluorochloromethylsulfenyl chloride, trichloromethylsulfenyl chloride does not add to ethylene [3].

EXPERIMENTAL

<u>Difluorochloromethyl β-chloroethyl sulfide.</u> Into a long test tube, from which all of the air had previously been displaced by ethylene, was charged a solution of 10 g of difluorochloromethylsulfenyl chloride [4] in 10 g of chloroform. The test tube was closed with a stopper that was fitted with both an inlet and an outlet tube. Ethylene from a gasometer was slowly passed through the inlet tube into the solution for 10 hr. The outlet tube was fitted with a stopcock and was connected to a Tishchenko flask containing sulfuric acid. Most of the reaction could be run with the stopcock on the outlet tube closed. Then the reaction mixture was fractionated through a column. Yield 7.5 g (64%). Colorless liquid with a disagreeable sulfide odor. The compound is insoluble in water, and is readily soluble in ether, chloroform and benzene.

B.P. 74° (76 mm), n_D^{19} 1.4474, d_4^{19} 1.4491.
Found %: C 19.88; H 2.56; S 17.90; F 21.94; Cl 38.98. $C_3H_4SF_2Cl_2$. Calculated %: C 19.81; H 2.20; S 17.70; F 21.90; Cl 39.21.

<u>Trifluoromethyl β-chloroethyl sulfide.</u> To a well-mixed mixture of 22 g of antimony trichloride and 1 g of antimony pentachloride in a glass flask was rapidly added 7.5 g of difluorochloromethyl β-chloroethyl sulfide, with stirring. Here the reaction mixture was cooled so that the temperature did not exceed 40°. When the evolution of heat had ceased, the mixture was distilled in an oil bath to remove the liquid reaction products, which were dried

over sodium sulfate, and then redistilled in a flask fitted with a short column. Yield 2.9 g (42.4%).

B.p. 96°, n_D^{16} 1.3960, d_4^{16} 1.4040.

Found %: C 21.84; H 2.50; S 19.68; F 34.73; Cl 21.70. $C_3H_4SF_3Cl$. Calculated %: C 21.88; H 2.44; S 19.45; F 34.60; Cl 21.63.

Trifluoromethylsulfenyl chloride. To a well mixed mixture of 60 g of antimony trichloride and 2 g of antimony pentachloride in a glass flask fitted with a reflux condenser, with cooling to 0°, was rapidly added 7.7 g of difluorochloromethylsulfenyl chloride. Then the flask was heated for 1 hr on the boiling-water bath, and the evolved gas was collected in a trap, cooled in liquid air. The obtained gases, about 4.1 g, were distilled through a column for low-boiling compounds, and began to boil at a temperature below -50°. The fraction with b.p. above -10° was collected. Analytically pure, trifluoromethylsulfenyl chloride has a boiling point of approximately 0°. From [1]: b.p. 0.7°. Yield 1.2 g (11.4%).

Found %: C 8.25; S 23.09; F 41.52; Cl 25.97. CSF_3Cl. Calculated %: C 8.80; S 23.44; F 41.75; Cl 26.01.

Iodine is liberated when trifluoromethylsulfenyl chloride is reacted with aqueous potassium iodide solution. Trifluoromethyl-(N-diethyl)sulfenamide is formed when the chloride is reacted with an ether solution of diethyl-amine.

Trifluoromethylsulfenyl bromide. Six grams of difluorobromomethylsulfenyl bromide [5] was added at room temperature to a well-mixed mixture of 15 g of antimony trifluoride and 1.5 g of antimony pentachloride. Here a small amount of heat was evolved. Then the reaction mixture was heated on the boiling-water bath to distill off the trifluoromethylsulfenyl bromide. The compound was obtained as a cherry-red liquid with an odor characteristic for alkylsulfenyl halides. It is hydrolyzed by water. Yield 2.48 g (41%).

B.p. 36°, n_D^{16} 1.3855, d_4^{16} 1.7704.

Found %: S 17.41; F 31.07; Br 44.10. CSF_3Br. Calculated %: S 17.67; F 31.61; Br 44.20.

SUMMARY

1. It was established that difluorochloromethylsulfenyl chloride, in contrast to trichloromethylsulfenyl chloride, is capable of adding to ethylene with the formation of difluorochloromethyl β-chloroethyl sulfide.

2. On the examples of reacting difluorochloromethylsulfenyl chloride, difluorobromomethylsulfenyl bromide and difluorochloromethyl β-chloroethyl sulfide with antimony trifluoride in the presence of catalysts it was shown that the difluorohalomethyl group exerts a stabilizing effect on the C—S linkage, in contrast to trichloromethyl-sulfenyl chloride.

LITERATURE CITED

[1] R. N. Haszeldine and J. M. Kidd, J. Chem. Soc. 1953, 3219.

[2] W. E. Truce, G. H. Birum and E. T. McBee, J. Am. Chem. Soc. 74, 3594 (1952; H. S. Booth and E. M. Bixby, Ind. Eng. Chem. 24, 637 (1932).

[3] I. B. Douglass, F. T. Martin and R. Addor, J. Org. Chem. 16, 1297 (1951).

[4] N. N. Yarovenko, S. P. Motornyi, A. S. Vasil'eva and T. P. Gershzon, Zhur. Obshchei Khim. 29, 2163 (1959)*

[5] N. N. Yarovenko and A. S. Vasil'eva, Zhur. Obshchei Khim. 29, 3792 (1959).*

*Original Russian pagination. See C. B. Translation.

FLUOROALKYL THIOCYANATES, ISOTHIOCYANATES, AND CARBYLAMINE HALIDES

N. N. Yarovenko, S. P. Motornyi, and L. I. Kirenskaya

Only 2-fluoroethyl thiocyanate, obtained by the reaction of 1-fluoro-2-bromoethane with potassium thiocyanate [1], is known in the series of fluorine-containing alkyl thiocyanates. We established that 1-fluoro-1-chloro-2-bromoethane, 1,1-difluoro-2-bromoethane and certain other polyhalogenated ethanes react with potassium thiocyanate in a similar manner. However, trihalomethyl thiocyanates cannot be obtained with this procedure. Only as recently as 1950 was it shown [2] that trichloromethyl thiocyanate can be obtained in good yield by reacting trichloromethylsulfenyl chloride with potassium cyanide. As was established by us, the reaction of potassium cyanide with fluorine analogs of trichloromethylsulfenyl chloride and with other fluorine-containing alkylsulfenyl halides proceeds in a similar manner.

The reaction of ether solutions of fluorodichloro- and difluorochloromethylsulfenyl chlorides, and also of β-chlorotetrafluoroethylsulfenyl chloride, with saturated aqueous potassium cyanide solution gave us the corresponding thiocyanates.

$$RSCL + KCN \rightarrow RSCN + KCl,$$
where R = $CFCl_2$, CF_2Cl, CF_2ClCF_2.
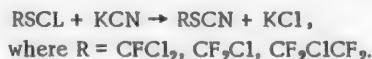
Polyhaloalkyl thiocyanates cannot be isomerized to the corresponding isothiocyanates, but some of the latter can be obtained in conventional manner by the reaction of halogenated primary amines with thiocarbonyl chloride (thiophosgene) [3].

The reaction of isothiocyanates with chlorine goes in two stages. The first stage is the addition of two chlorine atoms to the double bond, and it goes without the reaction mixture changing color. The start of the second stage is detected by an appearance of the color characteristic for sulfur dichloride.

$$CHF_2CH_2NH_2 \xrightarrow{CSCl_2} CHF_2CH_2N{=}C{=}S \xrightarrow{Cl_2} CHF_2CH_2N{=}C{\Big\langle}{}^{SCl}_{Cl} \xrightarrow{Cl_2}$$
$$\rightarrow CHF_2CH_2NCCl_2$$
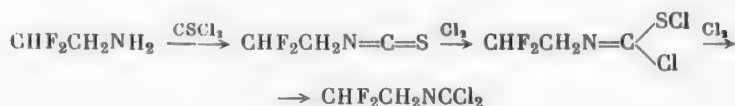
EXPERIMENTAL

Fluorodichloromethyl thiocyanate. A solution of 16 g of fluorodichloromethylsulfenyl chloride [4] in 30 ml of ether was cooled to 0°, and then with ice-water cooling and stirring, a solution of 9.9 g of potassium cyanide in 10 ml of water was added. The reaction mixture was stirred vigorously, with cooling in such manner that the temperature did not exceed 20°. Then, after the evolution of heat had ceased, the ether solution was separated, and the precipitate was washed several times with ether. The filtrate and rinse ether were combined, and after drying over sodium sulfate, the ether was distilled through a column, followed by distillation of the residue. Yield 9 g (56%).

B.p. 59° (80 mm), n_D^{18} 1.4661, d_4^{18} 1.5355.
Found %: C 15.28; N 8.77; S 19.80; F 11.97; Cl 44.40. C_2NSFCl_2. Calculated %: C 15.0; N 8.75; S 20.0; F 11.85; Cl 44.4.

The compound was obtained as a colorless liquid. It is insoluble in water, and readily soluble in ether, alcohol, benzene, and in other organic solvents.

Difluorochloromethyl thiocyanate. From 15.3 g of difluorochloromethylsulfenyl chloride [4] in 30 ml of ether and 9.9 g of potassium cyanide in 10 ml of water we obtained 8.8 g (58%) of the product.

B.p. 85°, n_D^{15} 1.4050, d_4^{15} 1.4221.

Found %: C 16.73; N 9.63; S 22.31; F 26.38; Cl 24.75. C_2NSF_2Cl. Calculated %: C 16.71; N 9.74; S 22.35; F 26.48; Cl 24.72.

The compound was obtained as a colorless liquid. It is insoluble in water, and readily soluble in the common organic solvents.

Tetrafluoro-2-chloroethyl thiocyanate. From 16 g of tetrafluoro-2-chloroethylsulfenyl chloride in 60 ml of ether and 6 g of potassium cyanide in 4 ml of water we obtained 11.5 g (74.5%) of the product.

B.p. 98°, n_D^{16} 1.3792, d_4^{16} 1.4769.
Found %: C 18.75; S 16.62; Cl 18.47. C_3NSF_4Cl. Calculated %: C 18.60; S 16.53; Cl 18.34.

2,2-Difluoroethyl thiocyanate. A mixture of 7.3 g of 2,2-difluoro-1-bromoethane, 4.8 g of potassium thiocyanate and 15 ml of alcohol was heated in a sealed ampule for 1 hr at 160°. Then the ampule was opened, the liquid was filtered, the alcohol was distilled off, and the residue was distilled. Yield 2.2 g (30%).

B.p. 96° (60 mm), n_D^{18} 1.4442, d_4^{18} 1.3434.
Found %: C 29.35; H 2.64; N 11.38; S 25.62; F 30.41. $C_3H_3NSF_2$. Calculated %: C 29.26; H 2.44; N 11.39; S 26.02; F 30.89.

2-Fluoro-2-chloroethyl thiocyanate. From 8 g of 1,1-fluorochloro-2-bromoethane, 4.8 g of potassium thiocyanate, and 15 ml of alcohol we obtained 2.5 g (30%) of the product.

B.p. 97° (25 mm), n_D^{21} 1.4875, d_4^{21} 1.3982.
Found %: C 26.18; H 1.98; N 10.06; S 23.08; F 13.96; Cl 25.53. C_3H_3NSFCl. Calculated %: C 25.81; H 2.15; N 10.03; S 22.94; F 14.33; Cl 25.44.

2,2-Difluoroethyl isothiocyanate. Into a three-necked flask, fitted with a mercury-seal stirrer and condenser, were charged a solution of 11.7 g of 2,2-difluoroethylamine hydrochloride in 10 ml of water and 40 ml of chloroform. Then a solution of 26 g of sodium carbonate in 120 ml of water and a solution of 11.5 g of thiophosgene in 10 ml of chloroform were added simultaneously in such manner that the reaction medium was always alkaline. When all of the reactants had been added, the reaction mass was stirred for an additional 30 min. A precipitate of sodium chloride gradually deposited during reaction, and the color of the solution changed from red to a light yellow. Then the precipitate was filtered and washed with chloroform. The chloroform solutions were combined, dried over sodium sulfate, and the whole then fractionally distilled through a column. Yield 6.6 g (52%).

B.p. 76° (100 mm), n_D^{25} 1.4725, d_4^{25} 1.3274.
Found %: C 28.91; H 2.69; N 11.44; S 25.80; F 30.82. $C_3H_3NSF_2$. Calculated %: C 29.26; H 2.44; N 11.38; S 26.01; F 30.82.

2,2-Difluoroethylcarbylamine chloride. Four grams of 2,2-difluoroethyl isothiocyanate was slowly saturated with chlorine, with cooling in such manner that the temperature in the reactor did not exceed 20°, until the weight increase due to chlorine was 4.6 g. Then the sulfur chlorides were distilled at a gauge pressure of 100 mm, followed by fractional distillation of the residue.

B.p. 63° (100 mm), n_D^{17} 1.4235, d_4^{17} 1.4726.
Found %: C 21.53; N 8.73; F 23.55; Cl 43.47. $C_3H_3NF_2Cl_2$. Calculated %: C 22.22; N 8.63; F 23.45; Cl 43.82.

The compound was obtained as a colorless liquid with an irritating odor. It is easily hydrolyzed by water, and is readily soluble in ether and chloroform.

SUMMARY

1. It was shown that fluoroalkyl thiocyanates are obtained by the reaction of fluorinated alkylsulfenyl halides with potassium cyanide.

2. The synthesis of some new compounds in the series of fluorinated alkylthiocyanates, isothiocyanates, and carbylamine halides was described. These compounds are fluorodichloromethyl, difluorochloromethyl, tetrafluoro-2-chloroethyl, 2,2-difluoroethyl and 2-fluoro-2-chloroethyl thiocyanates, 2,2-difluoroethyl isothiocyanate, and 2,2-difluoroethylcarbylamine chloride.

LITERATURE CITED

[1] B. C. Saunders, G. J. Stacey, and I. G. E. Wilding, J. Chem. Soc. 1949, 773.

[2] H. Brintzinger, K. Pfannstiel, H. Koddebusch, and K. E. Kling, Ber. 83, 87 (1950); U. S. Patent, 2, 650, 240, 240 (1953); C. A. 48, 8819 (1954).

[3] H. Brintzinger, K. Pfannstiel, and H. Koddebusch, Ber. 82, 389 (1949).

[4] N. N. Yarovenko, S. P. Motornyi, A. S. Vasil'eva, and T. P. Gershzon, Zhur. Obshchei Khim. 29, 2163 (1959).*

---

*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF DIFLUORO- AND FLUOROCHLOROTHIOCARBONYLS AND THEIR PROPERTIES

N. N. Yarovenko and A. S. Vasil'eva

It has been shown previously [1] that 2-chlorotetrafluoroethylsulfur chloride reacts easily with metallic tin, under the conditions usual for the preparation of thiocarbonyl chloride from trichloromethylsulfur chloride, with the formation of difluorochlorothioacetyl fluoride.

$$CF_2ClCF_2SCl \xrightarrow{Sn} CF_2ClC{\overset{S}{\underset{F}{\big\langle}}}$$
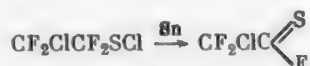
In the present communication, we present similar reactions of fluorine analogs of trichloromethylsulfur chloride with metallic tin and describe the chemical properties of difluorothiocarbonyl and fluorochlorothiocarbonyl.

As is well known, difluorothiocarbonyl cannot be prepared by the fluorination of thiocarbonyl chloride. When thiocarbonyl chloride is reacted with hydrogen fluoride or with the fluorides of antimony, zinc, lead, or silver (in some cases in the presence of catalysts), fluorochloromethanes are formed. Thus, for example, when vapors of thiocarbonyl chloride are passed over lead fluoride at $170-250°$, difluorodichloromethane is produced [2].

$$CSCl_2 \xrightarrow{[PbF_2]} CF_2Cl_2$$

When carbon bisulfide is reacted with hydrogen fluoride and chlorine or with antimony fluorides in the presence of catalysts, and also with the fluorides of some other elements, all the C—S bonds are ruptured and fluorochloromethanes are formed [2, 3].

$$CS_2 \xrightarrow{SbF_3Cl_2} CFCl_3 + CF_2Cl_2 + CF_3Cl$$

Difluorothiocarbonyl was mentioned for the first time by Ruff (cf. [4]), who assumed that he had obtained this compound by the reaction of carbon bisulfide with iodine pentafluoride. However, Hazeldine [4] showed that the product that Ruff took for difluorothiocarbonyl was actually thionyl fluoride. The formation of difluorothiocarbonyl was further observed when trifluoroiodomethane was reacted with elementary sulfur [5, 6] and when carbon bisulfide was fluorinated with elemental fluorine [7]. However, in no case was difluorothiocarbonyl obtained in the pure form. No one had attempted to prepare difluorothiocarbonyl starting with difluorochloromethylsulfur chloride, i.e., with a compound already simultaneously containing atoms of fluorine, sulfur, and carbon. As we have established, difluorochloromethylsulfur chloride and fluorodichloromethylsulfur chloride react with tin under considerably milder conditions than trichloromethylsulfur chloride. While the reaction of trichloromethylsulfur chloride with tin starts when the reaction mixture is heated almost to boiling, the reaction of difluorochloromethylsulfur chloride with the same metal starts at room temperature. The reaction of fluorodichloromethylsulfur chloride with tin starts with slight heating.

$$CFCl_2SCl \xrightarrow{Sn} {\overset{F}{\underset{Cl}{\big\rangle}}}C=S$$

$$CF_2ClSCl \xrightarrow{Sn} {\overset{F}{\underset{F}{\big\rangle}}}C=S$$
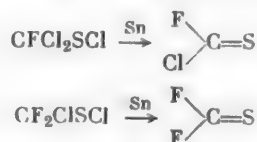
The structure of the fluorine analogs of thiocarbonyl chloride was confirmed by a series of reactions. Difluoro-thiocarbonyl, and also fluorochlorothiocarbonyl, readily add bromine to form difluorobromomethylsulfur bromide and fluorochlorobromomethylsulfur bromide, respectively.

$$\underset{Cl}{\overset{F}{>}}C=S \xrightarrow{Br_2} CFClBrSBr$$

$$\underset{F}{\overset{F}{>}}C=S \xrightarrow{Br_2} CF_2BrSBr$$
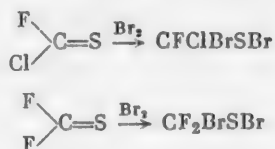
When the fluorine analogs of thiocarbonyl chloride react with alcohols, thioalcohols, and amines, the esters, thioesters, and amides of fluorothiocarbonic acid are formed, respectively.

$$\underset{Hal}{\overset{F}{>}}C=S \begin{cases} \xrightarrow{ROH} & RO-C\overset{S}{\underset{F}{\diagdown}} \\ \xrightarrow{R'SH} & R'S-C\overset{S}{\underset{F}{\diagdown}} \\ \xrightarrow{R''_2NH} & R''_2N-C\overset{S}{\underset{F}{\diagdown}} \end{cases}$$
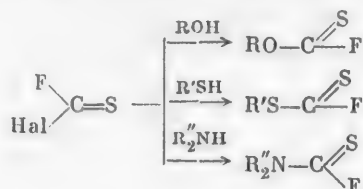
EXPERIMENTAL

Fluorochlorothiocarbonyl. In a round-bottomed flask fitted with a dropping funnel and reflux condenser were placed 13.5 g of granulated tin and 30 ml of 28% hydrochloric acid. The mixture was heated to slight boiling, after which the addition of 16.9 g of fluorodichloromethylsulfur chloride [8] was started from the separatory funnel, the end of which reached to the bottom of the reaction flask. The reduction should not be carried out too vigorously. The gases evolved passed through the reflux condenser and were condensed in a trap cooled with a mixture of acetone and solid carbon dioxide. Then the mixture of products obtained, consisting of hydrogen chloride, fluorochlorothio-carbonyl, and fluorodichloromethylsulfur chloride, was distilled on a column for low-boiling materials. The yield of fluorochlorothiocarbonyl was 8.5 g (87%). B.p. 9°.

Found %: C 11.89; S 31.84; F 19.36; Cl 36.04. CSFCl. Calculated %: C 12.18; S 32.49; F 19.29; Cl 36.04.

The fluorochlorothiocarbonyl was a gas with a very beautiful yellow color. On cooling, it condensed to a liquid, also of a yellow color. The fluorochlorothiocarbonyl dissolved well in ether, chloroform, and benzene. It reacted vigorously with alcohols, thioalcohols, and amines. It freed iodine from potassium iodide. It was hy-drolyzed by water slowly at 0°, but at room temperature the hydrolysis proceeded considerably more rapidly.

Difluorothiocarbonyl. In a round-bottomed flask fitted with a reflux condenser and dropping funnel were placed 5 g of granulated tin and 10 ml of 28% hydrochloric acid, and 6 g of difluorochloromethylsulfur chloride was added slowly [8]. The reaction proceeded with the evolution of heat. The gases evolved were collected in a trap cooled with liquid air. The reduction of difluorochloromethylsulfur chloride should not be carried out too vigorously. The difluorothiocarbonyl thus obtained contained up to 6% of hydrogen chloride and some carbon bi-sulfide as a contaminant, of which it was freed by redistillation of the gases on a column for low-boiling materials. The yield of difluorothiocarbonyl was 1.52 g (47.5%). B.p. from -57 to -54°.

Found %: C 14.52; S 39.82; F 45.82. CSF$_2$. Calculated %: C 14.64; S 39.02; F 46.34.

The difluorothiocarbonyl was a colorless gas. It dissolved well in ether, chloroform, and benzene. It reacted vigorously with alcohols, thioalcohols, and amines. It was readily hydrolyzed by water.

Difluorobromomethylsulfur bromide. To 1 g of difluorothiocarbonyl, cooled in an ampule with liquid air, was added 2 g of bromine. Then the ampule was sealed and slowly warmed to room temperature, when the reaction mixture became considerably lighter and took on a cherry red color. The reaction proceeded with considerable evolution of heat. The contents of the ampule were shaken and allowed to stand at room temperature for 20—30 minutes. Then the ampule was opened and the difluorobromomethylsulfur bromide was distilled. The yield of difluorobromomethylsulfur bromide was 1.6 g (55.5%).

B.p. 107°, n_D^{17} 1.5210, d_4^{17} 2.3550.

Found %: C 4.99; S 13.24; F 15.88; Br 65.41. CSF_2Br_2. Calculated %: C 4.97; S 13.22; F 15.70; Br 66.11.

The difluorobromomethylsulfur bromide was a liquid with a cherry red color. The odor was characteristic of alkylsulfur halides. It was readily hydrolyzed by water.

Fluorochlorobromomethylsulfur bromide. The reaction of fluorochlorothiocarbonyl with bromine was carried out under the same conditions as for the reaction of difluorothiocarbonyl with bromine. From 7 g of fluorochloro-thiocarbonyl and 11.3 g of bromine there was obtained 14.8 g of fluorochlorobromomethylsulfur bromide (81%).

B.p. 134° (decomp.), n_D^{18} 1.5616, d_4^{18} 2.3676.

Found %: C 5.04; S 12.86; F 7.21; Cl + Br 75.97. $CSFClBr_2$. Calculated %: C 4.65; S 12.39; F 7.36; Cl + Br 75.60.

The fluorochlorobromomethylsulfur bromide was a liquid with a cherry red color. The odor was characteristic of alkylsulfur halides. It was readily hydrolyzed by water.

Reaction of fluorochlorothiocarbonyl with alcohols. a) With methyl alcohol. In a glass test tube fitted with a dropping funnel and a delivery tube connected to a wash bottle with sulfuric acid was placed 5.5 g of fluoro-chlorothiocarbonyl and, while the mixture was cooled with liquid air, 1.5 g of methyl alcohol was added dropwise. Then the reaction mixture was slowly warmed,while being shaken, to 0°, kept at this temperature for several hours until the evolution of hydrogen chloride had almost ceased, and then left overnight at room temperature. The next day the mixture was dried with sodium sulfate and the methyl ester of fluorothiocarbonic acid was distilled off on a column. The yield was 1.7 g (38.3%).

B.p. 66° (755 mm), n_D^{17} 1.4170, d_4^{17} 1.1900.

Found %: C 25.50; H 3.92; S 34.08; F 20.16. C_2H_3OSF. Calculated %: C 25.53; H 3.20; S 34.04; F 20.21.

b) With ethyl alcohol. The reaction of fluorochlorothiocarbonyl with ethyl alcohol was carried out under the same conditions as for its reaction with methyl alcohol. From 8 g of fluorochlorothiocarbonyl and 3 g of ethyl alcohol there was obtained 3 g (43%) of the ethyl ester of fluorothiocarbonic acid.

B.p. 84° (755 mm), n_D^{17} 1.4200, d_4^{17} 1.1020.

Found %: C 32.72; H 4.50; S 30.20; F 17.40. C_3H_5OSF. Calculated %: C 33.33; H 4.63; S 29.63; F 17.59.

c) With isopropyl alcohol. The reaction of fluorochlorothiocarbonyl with isopropyl alcohol was carried out under the same conditions as for its reaction with methyl alcohol. From 7 g of fluorochlorothiocarbonyl and 3 g of isopropyl alcohol there was obtained 2.9 g (47.4%) of the isopropyl ester of fluorothioacetic acid.

B.p. 78° (750 mm), n_D^{17} 1.4110, d_4^{17} 0.9990.

Found %: C 39.10; H 6.04; S 26.36; F 15.34. C_4H_7OSF. Calculated %: C 39.34; H 5.74; S 26.23; F 15.57.

Reaction of fluorochlorothiocarbonyl with phenol. A solution of 13.5 g of phenol and 5.7 g of sodium hydroxide in 120 ml of water cooled to -5° was added dropwise, with energetic stirring, to a solution of 14 g of fluorochloro-thiocarbonyl in 50 ml of chloroform cooled to -5°. The reaction was carried out with cooling so that the tempera-ture of the reaction mixture did not rise above 0°. Then the lower layer was separated off, dried with calcium chloride, the chloroform was distilled off, and the phenyl ester of fluorothiocarbonic acid was distilled. The yield was 8 g (36%).

B.p. 87° (40 mm), n_D^{19} 1.5260, d_4^{19} 1.2048.

Found %: C 53.83; H 3.74; S 19.77; F 12.58. C_7H_5OSF. Calculated %: C 53.84; H 3.20; S 20.51; F 12.17.

Reaction of fluorochlorothiocarbonyl with mercaptans. a) With methyl mercaptan. In a glass flask fitted with a delivery tube connected to a wash bottle with sulfuric acid was placed 9 g of fluorochlorothiocarbonyl, and 4.5 g of methyl mercaptan was added while the mixture was cooled with liquid air. Then, while the reaction mixture was stirred, it was slowly warmed to 0°, kept at that temperature for 2–3 hours, and left overnight at room tempera-ture. The next day the reaction mixture was distilled at reduced pressure, washed with water, dried with sodium sulfate, and the methyl ester of dithiofluorocarbonic acid was distilled.

B.p. 78° (240 mm), n_D^{18} 1.5545, d_4^{18} 1.200.

Found %: C 22.08; H 3.04; S 58.84; F 16.79. $C_2H_3S_2F$. Calculated %: C 21.82; H 2.73; S 58.18; F 17.27.

b) With ethyl mercaptan. The reaction of fluorochlorothiocarbonyl with ethyl mercaptan was carried out under the same conditions as for its reaction with methyl mercaptan. From 8 g of fluorochlorothiocarbonyl and 5 g of ethyl mercaptan there was obtained 9 g (89.5%) of the ethyl ester of dithiofluorocarbonic acid.

B.p. 73° (93 mm), n_D^{15} 1.5041, d_4^{15} 1.1736.
Found %: C 29.31; H 4.18; S 52.36; F 15.83. $C_3H_5S_2F$. Calculated %: C 29.03; H 4.04; S 51.51; F 15.32.

Reaction of fluorochlorothiocarbonyl with diethylamine. To a solution of 7.5 g of fluorochlorothiocarbonyl in 10 ml of ether, cooled with liquid air, was added 8.5 g of diethylamine in 10 ml of ether, and while the mixture was stirred, it was slowly warmed to room temperature. After the reaction had ended, the ether solution was separated from the diethylamine hydrochloride, the ether was distilled off, and the diethylamide of fluorothiocarbonic acid was distilled. The yield was 3.5 g (45%).

B.p. 100° (21 mm), n_D^{15} 1.4790, d_4^{15} 1.0580.
Found %: C 44.28; H 7.40; N 10.49; S 23.65; F 13.83. $C_5H_{10}NSF$. Calculated %: C 44.44; H 7.42; N 10.37; S 23.70; F 14.07.

SUMMARY

1. A method has been described for the preparation of difluorothiocarbonyl and fluorochlorothiocarbonyl by the reduction of difluorochloromethylsulfur chloride and fluorodichloromethylsulfur chloride, respectively.

2. The products of the reaction of the fluorine analogs of thiocarbonyl chloride with bromine, alcohols, thioalcohols, and amines have been described.

LITERATURE CITED

[1] N. N. Yarovenko, S. P. Motornyi, L. I. Kirenskaya, and A. S. Vasil'eva, J. Gen. Chem. 27, 2243 (1957).*

[2] Amer. Patent 2004932; Zbl. 1936, I, 875.

[3] Engl. Patent 454577; Zbl. 1937, I, 1013; Engl. Patent 463970; Zbl. 1937, II, 1445.

[4] R. N. Haszeldine and J. M. Kidd, J. Chem. Soc. 1953, 3219.

[5] F. N. Bennett, G. R. Brandt, H. J. Emeleus, and R. N. Haszeldine, Nature 166, 225 (1950).

[6] G. A. Brandt, H. J. Emeleus and R. N. Haszeldine, J. Chem. Soc. 1952, 2198.

[7] E. A. Pyczkowski and L. A. Bigelow, J. Am. Chem. Soc. 75, 3523 (1953).

[8] N. N. Yarovenko, S. P. Motornyi, A. S. Vasil'eva, and T. P. Gershzon, J. Gen. Chem. 29, 2163 (1959).*

* Original Russian pagination. See C. B. translation.

INVESTIGATION IN THE FIELD OF ALKANESULFONIC ACIDS

XXI. SYNTHESIS AND CHLORINATION OF ALKANESULFONITROANILIDES

A. G. Kostsova

Voronezh State University

We have described the synthesis and properties of p-nitroanilides of some alkanesulfonic acids, but the yields of these compounds did not exceed 11% [1]. Therefore we attempted to find the optimum conditions for their synthesis. It was found that the reaction conditions previously used by us were too mild. The best results were obtained if the reaction was carried out in pyridine with prolonged heating (10—11 hours) of the alkanesulfonyl chloride and p-nitroaniline at 140—160°; under these conditions the yields of the p-nitro anilides reached 60—68%. The synthesis of the o- and m-nitroanilides was carried out for the first time in our work.

It has been shown that nitroanilines react with alkanesulfonyl chlorides with incomparably more difficulty than unsubstituted aniline, toluidine, anisidine, and the like [2]; however, of the three isomers, m-nitroaniline reacts the most easily, p-nitroaniline with more difficulty, and o-nitroaniline practically does not react. These observations are in full agreement with the facts, since the electron acceptor effect of the nitro group is more efficiently transmitted by the benzene ring from the ortho- and para- positions than from the meta- position, which is explained as a special case of the reciprocal effect of atoms— a conjugation effect [3].

The chlorination of the nitroanilides has been studied for the p- and m- nitroanilides of ethane- and butane-sulfonic acids. The experiments showed that the conditions used by us for the chlorination of the anilides [4], toluidides [5], anisidides [6], and the like were not appropriate in this case. However, if the chlorination (for example, of the p-nitroanilides) was carried out in the presence of $AlCl_3$ with the reaction mixture boiling, then the monochloro-p-nitroanilide was formed in which the chlorine occupied the ortho-position in relation to the alkyl-sulfonamide group and the meta-position to the nitro group. In this case there was a concordance of orientation, as a result of which only the one isomer of the monochloro derivative was formed. The position of the chlorine in the ring was demonstrated by hydrolysis of the monochloro-p-nitroanilides to 2-chloro-4-nitroaniline, the properties and constants of which were known in the literature [7]. The chlorination and subsequent hydrolysis can be represented by the following diagram.
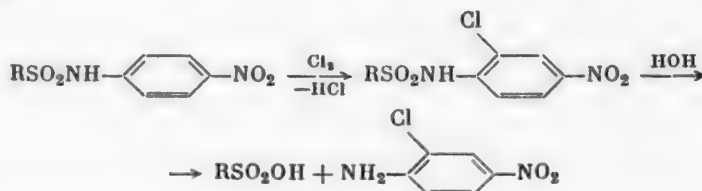
The chlorination of the m-nitroanilides took place more easily than that of the p-nitroanilides, and butane-sulfo-m-nitroanilide was chlorinated in dichloroethane and dioxane in the absence of a catalyst. Ethanesulfo-m-nitroanilide was chlorinated only in the presence of $AlCl_3$ but more rapidly and with less catalyst than the p-nitro-anilide, with a yield of up to 80%. The products formed in the chlorination of the m-nitroanilides had broad melting and boiling points, but analysis for nitrogen, chlorine, and sulfur indicated the monochloro derivative. From this it should be concluded that in this case not individual compounds, but a mixture of isomeric monochloro-m-nitroanilides was formed, since the meta-position of the nitro group in relation to the alkylsulfonamide group leads

to a discordance in the orientation of the chlorine, which is the cause of the formation of the isomers. We did not succeed in separating this mixture. Some data on the compounds obtained are given in the table.

Expt. No.	Name and Formula	Empirical Formula	% N		% Cl		% S	
			found	calculated	found	calculated	found	calculated
1	Ethanesulfo-m-nitroanilide	$C_8H_{10}O_4N_2S$	11.95	12.17	—	—	14.02	13.91
2	Butanesulfo-m-nitroanilide	$C_{10}H_{14}O_4N_2S$	10.81	10.85	—	—	12.45	12.40
3	Ethanesulfo-2-chloro-4-nitro-anilide	$C_8H_9O_4N_2SCl$	10.54	10.58	13.12	13.42	11.92	12.09
4	Butanesulfo-2-chloro-4-nitro-anilide	$C_{10}H_{13}O_4N_2SCl$	9.62	9.60	11.95	12.13	10.97	10.94
5	Ethanesulfo-monochloro-m-nitroanilide (mixture of isomers)	$C_8H_9O_4N_2SCl$	10.44	10.58	12.98	13.42	11.98	12.09
6	Butanesulfo-monochloro-m-nitroanilide (mixtures of isomers)	$C_{10}H_{13}O_4N_2SCl$	9.51	9.60	11.72	12.13	10.82	10.94

EXPERIMENTAL

Preparation of nitroanilides. In a round-bottomed flask fitted with a two-branched adapter, in the straight branch of which a thermometer was placed, and the side branch of which was connected to a condenser, was mixed 10.8 g of ethanesulfonyl chloride, 13.8 g of p-nitroaniline, and 50 ml of pyridine. The mixture was heated at first on a water bath for 2 hours, and then on a paraffin bath for 11 hours at 150—160°. At the end of the reaction, the mixture was left until the following day. Further treatment and isolation of the reaction product were carried out by the method previously described by us [1]. The yield of ethanesulfo-p-nitroanilide was 12.2 g (65.6%). To prepare butanesulfo-p-nitroanilide, 12 g of butanesulfonyl chloride, 11.5 g of p-nitroaniline, and 40 ml of pyridine were used. The yield of the product was 13.5 g (68.5%).

The m-nitroanilides were prepared by heating on the water bath for 2 hours and then on a paraffin bath at 100—120° for 3 hours. From 22.5 g of ethanesulfonyl chloride, 29 g of m-nitroaniline, and 40 ml of pyridine there was obtained 27.4 g (68.2%) of ethanesulfo-m-nitroanilide. M.p. 139—141° (from aqueous alcohol). To prepare butanesulfo-m-nitroanilide, 19 g of butanesulfonyl chloride, 17 g of m-nitroaniline, and 40 ml of pyridine were used. The product was isolated as a thick brown oil, which crystallized only after standing for many days. M.p. 64—66° (from aqueous alcohol). The yield was 22 g (70.5%).

Chlorination of nitroanilides. a) Two g of ethanesulfo-p-nitroanilide in 55 ml of dichloroethane and 1.8 g of $AlCl_3$ (1:1.5) were mixed in a round-bottomed flask fitted with a two-branched adapter, one branch of which was connected to a condenser and the other to a gas outlet tube that was connected to a drying bottle filled with sulfuric acid, and the latter connected to a rheometer that regulated the rate of passage of chlorine from a gas cylinder. The reaction mixture was heated to boiling and the chlorine was passed through at the rate of 3.3 ml/sec for 2 hours. The next day, the contents of the flask were treated with ice water acidified with hydrochloric acid. The stratified liquid was separated; the dichloroethane layer was washed with water, separated, and transferred to a porcelain dish for evaporation. A dark crystalline mass remained as a residue. The crystals were washed twice with small portions of cold alcohol to remove traces of unreacted nitroanilide, and then the washed chlorination product was recrystallized from hot alcohol. When the solution was cooled, slightly yellowish, fibrous crystals of the monochloro-p-nitroanilide of ethanesulfonic acid separated out. The yield of the product was 1.8 g (78.3%). M.p. 115—116° (from hot alcohol).

b) For the chlorination of butanesulfo-p-nitroanilide, 2 g of p-nitroanilide in 15 ml of dichloroethane and 1.15 g of $AlCl_3$ (1:1) were used and chlorine was passed through for 2 hours at the rate of 3.3 ml/sec, while the

reaction mixture was heated on a water bath. The yield was 1.5 g (68%). M.p. 80—82° (from hot alcohol).

c) Two g of ethanesulfo-m-nitroanilide in 40 ml of dichloroethane and 1.15 g of AlCl₃ (1:1) were chlorinated at boiling for 1 hour. Further treatment and isolation of the product were carried out in a similar manner to the preceding. The yield of product was 1.8 g (78.2%). M.p. 63—70° (from aqueous alcohol).

d) Two g of butanesulfo-m-nitroanilide in 15 ml of dichloroethane and 1.15 g of AlCl₃ (1:1) were used. The reaction conditions were similar to the preceding experiment. The chlorination product that was isolated was a heavy reddish oil, which was dissolved in ether, the ether solution was dried with potassium carbonate, then the ether was distilled off, and the oil was distilled in vacuo at 140—190° (5 mm). In this case also, an individual product was not formed.

All the nitroanilides were chlorinated also under other conditions: without a catalyst, in the presence of ZnO, in dioxane without and with a catalyst, with and without heating. Under the indicated conditions only butanesulfo-m-nitroanilide was chlorinated to form the oily chlorination product mentioned above; the other nitroanilides remained unchanged.

Hydrolysis of monochloro-p-nitroanilides of ethane- and butanesulfonic acids. The hydrolysis was carried out by the method previously described by us [4]. 0.3 g of butanesulfo-p-nitroanilides was used. The reaction went very slowly and was over in 34—36 hours. In the hydrolysis, partial resinification was observed, therefore after dilution with water, the reaction mixture was filtered off from the tarry contaminants. The clear, light-yellow filtrate was made alkaline. The yellow flocculent precipitate that separated out was extracted with ether, the ether extract was dried with potassium carbonate, and the ether was partially distilled off. The remainder was poured into a dish. The bright yellow 2-chloro-4-nitroaniline was isolated by evaporating the ether. The yield was 0.10 g (58.82%). M.p. 103—105° (from aqueous alcohol); according to the data in [7], m.p. 105°. Analysis for nitrogen also agreed with this compound. Hydrolysis of ethanesulfo-2-chloro-p-nitroanilide also gave the same compound.

SUMMARY

The method for the preparation of alkanesulfonitroanilides has been improved Ethane- and butane sulfonitroanilides have been prepared and characterized for the first time. A method has been developed for the chlorination of alkanesulfonitroanilides; the monochloronitroanilides of ethane- and butanesulfonic acids have been prepared and characterized.

The structure of the monochloro-p-nitroanilides was demonstrated by hydrolysis. The effect of the nitro group on the reactivity of the aromatic nucleus in the nitroanilines and alkanesulfonitroanilides has been shown.

LITERATURE CITED

[1] A. G. Kostsova, J. Gen. Chem. 24, 618 (1954).*

[2] A. G. Kostsova, J. Gen. Chem. 22, 1433 (1952).*

[3] O. A. Reutov, Theoretical Problems of Organic Chemistry [in Russian] (izd. MGU, 1956) p. 58.

[4] A. G. Kostsova, N. M. Yanova, and Z. N. Sushko, J. Gen. Chem. 26, 2855 (1956).*

[5] A. G. Kostsova and N. T. Borisova, J. Gen. Chem. 28, 2420(1958).*

[6] A. G. Kostsova, J. Gen. Chem. 28, 1573 (1958).*

[7] Dictionary of Org. Compounds 1 [in Russian] p. 500.

Received October 31, 1958

---

* Original Russian pagination. See C. B. translation.

INVESTIGATION IN THE FIELD OF ALKANESULFONIC ACIDS

XXII. BROMINATION OF N-ARYLAMIDES OF ALKANESULFONIC ACIDS

A. G. Kostsova,

Voronezh State University

In the development of the previously described work on the chlorination of the N-arylamides of alkanesulfonic acids [1], we have undertaken the bromination of these compounds in dichloroethane by mixing solutions of the N-arylamide and bromine at room temperature. A rise in temperature was not observed in this case such as occurs in the chlorination.

As the experiments showed, the anilides are brominated to the p-bromoanilides and the p- and o-toluidides to the monobromotoluidides, where in the p-toluidides the bromine occupies the ortho-position to the alkylsulfonamide group, and in the o-toluidides it occupies the para-position to this group. The tetrabromotoluidides are not formed here, in contrast to the chloro derivatives. The anisidides, even with a deficiency of bromine, are brominated to form the dibromoanisidides. Tetrabromoquinone and tetrabromoanisidide have not been detected. It must be noted that the o-anisidides are brominated better under various conditions than the p-anisidides, with the formation of pure products in high yields, while the brominated p-anisidides, as a rule, are contaminated with unreacted p-anisidide. The nitroanilides are practically unbrominated under the given conditions, even in the presence of $AlCl_3$, and on heating, only traces of the bromo derivatives are found.

The position of the bromine in the ring was demonstrated by hydrolysis to the corresponding bromoamine, although this was not successful in all cases. Thus, for example, the dibromo-p- and o-anisidides are not all described in the literature, and therefore it was necessary to judge the structure of the dibromoanisidides obtained by us from the hydrolysis by analogy with the chloro derivatives of the same compounds [1].

All the bromination reactions can be expressed by the following equations.
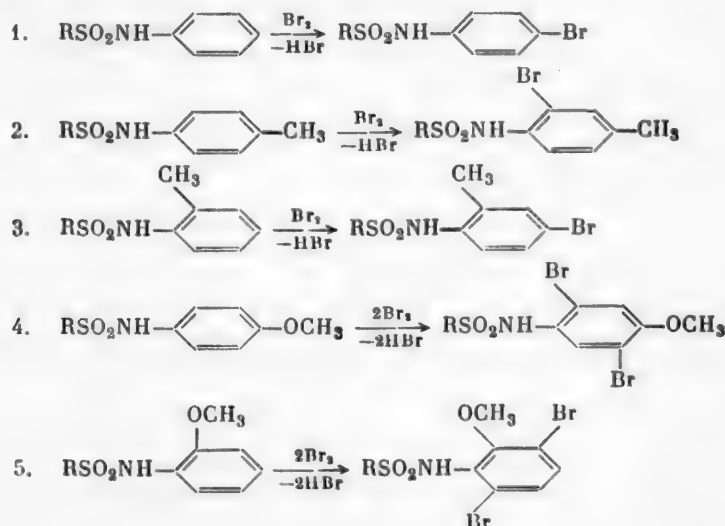
We carried out the bromination of these same N-arylamides with the aid of dioxane dibromide [2]. The anilides and toluidides were brominated by mixing their ether solutions with an ether solution of dioxane dibromide; the anisidides are not brominated under these conditions; however, the reaction takes place if it is carried out by melting the components at 70—80° in the absence of solvents, with the p-anisidides being brominated considerably less satisfactorily than the o-anisidides. As shown by the experiments, on bromination with dioxane dibromide the same products are formed as in direct bromination, but with lower yields; a considerable part of the starting N-arylamide is isolated from the reaction unchanged. The anilide and the toluidides of methanesulfonic acid are brominated better than the others by this method.

The bromo derivatives of the N-arylamides of the alkanesulfonic acids are colorless crystalline compounds, readily soluble in alkalies, dichloroethane, acetone, ether, and benzene; soluble in alcohol only on heating (this fact has been utilized to purify them from the starting N-arylamides, which are readily soluble in cold alcohol); they are insoluble in water. The compounds obtained (Table 1) are of interest as possible pharmaceutical preparations.

EXPERIMENTAL

The bromination of all the N-arylamides was carried out by the same method. The experimental data are given in Table 2.

a) The N-arylamide was dissolved in dichloroethane. The bromine, dissolved in 5—10 ml of dichloroethane, was added in portions, with stirring. In a few minutes copious evolution of H3r started, but the temperature of the reaction mixture did not rise. After two hours of stirring, the mixture was left until the following day, and then it was transferred to a dish for evaporation. The residue was washed with water, then with alcohol. Recrystallization was carried out from hot alcohol. In the case of the bromination of the p-anisidides, there was an appreciable amount of the starting anisidide in the reaction products, which was removed by washing three times with cold alcohol.

TABLE 1

Name and Empirical Formula	Melting point	% N		% Br		% S	
		found	calcu-lated	found	calcu-lated	found	calcu-lated
1. Methanesulfo-4-bromoanilide $C_7H_8O_2NSBr$	134—135°	5.54	5.60	31.91	32.00	12.84	12.80
2. Ethanesulfo-4-bromoanilide $C_8H_{10}O_2NSBr$	100—102	5.25	5.30	29.96	30.30	11.88	12.12
3. Methanesulfo-3-bromo-p-toluidide $C_8H_{10}O_2NSBr$	85—86	5.43	5.30	30.35	30.30	11.95	12.12
4. Ethanesulfo-3-bromo-p-toluidide $C_9H_{12}O_2NSBr$	51—53	4.95	5.03	28.56	28.77	11.62	11.51
5. Methanesulfo-5-bromo-o-toluidide $C_8H_{10}O_2NSBr$	139—140	5.21	5.30	30.40	30.31	12.86	12.12
6. Ethanesulfo-5-bromo-o-toluidide $C_9H_{12}O_2NSBr$	114—116	5.12	5.03	28.79	28.77	11.44	11.51
7. Methanesulfo-2,5-dibromo-p-anisidide $C_8H_9O_3NSBr_2$	153—155	3.90	3.90	44.21	44.50	9.02	8.93
8. Ethanesulfo-2,5-dibromo-p-anisidide $C_9H_{11}O_3NSBr_2$	146—148	3.68	3.75	42.55	42.89	8.61	8.57
9. Methanesulfo-3,6-dibromo-o-anisidide $C_8H_9O_3NSBr_2$	131—132	3.40	3.90	44.25	44.50	8.81	8.93
10. Ethanesulfo-3,6-dibromo-o-anisidide $C_9H_{11}O_3NSBr_2$	105—107	3.42	3.75	42.80	42.89	8.50	8.57
11. Butanesulfo-2,5-dibromo-p-anisidide $C_{11}H_{15}O_3NSBr_2$	87—89	3.41	3.49	40.01	39.90	7.82	7.98

b) Ether solutions of the N-arylamide and dioxane dibromide were mixed. The mixture was left until the following day, and then it was washed with water. The ether layer was separated off, dried with potassium carbonate, and the ether was evaporated. The remaining yellowish crystals were recrystallized from hot alcohol. The bromination of ethanesulfo-o-toluidide with dioxane dibromide yielded a product highly contaminated with the starting o-toluidide. By repeated washing with ether, and then with alcohol, with subsequent recrystallization from the latter, it was possible to obtain a pure product, but in very low yield. Bromination of the anisidides with dioxane dibromide in ether or dioxane did not take place, and it therefore was carried out by melting the anisidide with the dioxane dibromide at 70—80° for 12—15 minutes. The fusion was poured into a beaker of water. The solidified mass was separated off, washed several times with water, and then with alcohol from the unreacted anisidide (the para-isomer, as a rule, was more contaminated than the ortho-isomer). The results of the bromination of the N-arylamides of the alkanesulfonic acids are given in Table 2.

Hydrolysis of the brominated N-arylamides of alkanesulfonic acids was carried out by the method described previously [1]. In all cases 0.3 g of the compound was used. When methane- and ethanesulfo-4-bromoanilides were hydrolyzed, p-bromoaniline was isolated with m.p. 64—65°; when methane- and ethanesulfo-3-bromo-p-toluidides were hydrolyzed, 3-bromo-p-toluidine was separated as an oil and converted to the N-acetyl derivative with m.p. 116—117°; when the 5-bromo-o-toluidides were hydrolyzed, N-acetyl-5-bromo-o-toluidine was obtained with m.p. 155—157°; when the dibromo-p-anisidides were hydrolyzed, probably the 2,5-dibromo-p-anisidine, which is not described in the literature, was formed with m.p. 78—80° (by analogy with the hydrolysis of the di-chloro-p-anisidides [1]); and finally, when the dibromo-o-anisidides were hydrolyzed, dibromo-o-anisidine with m.p. 97-99° was produced.

TABLE 2

| Name | Bromination of N-Arylamides | | | | | | | |
| | with Bromine | | | | with Dioxane Dibromide | | | |
	N-aryl-amide (g)	bromine (g)	solvent (ml)	yield (%)	N-aryl-amide (g)	dioxane dibro-mide (g)	solvent (g)	yield (%)
1. Methanesulfonanilide	1.5	1.4	30	70.0	0.5	0.72	25	68.5
2. Ethanesulfonanilide	1.2	1.1	30	87.7	1.6	4.8	40	43.8
3. Methanesulfo-p-toluidide	1.5	1.3	30	91.3	2.0	3.0	40	87.6
4. Methanesulfo-o-toluidide	1.5	1.3	30	88.9	2.0	3.0	35	84.1
5. Ethanesulfo-p-toluidide	1.5	1.2	30	86.1	0.5	0.6	20	44.9
6. Ethanesulfo-o-toluidide	1.0	0.8	20	72.0	1.0	1.2	25	11.2
7. Methanesulfo-p-anisidide	1.0	1.6	35	57.5	1.0	2.0	fused	28.7
8. Methanesulfo-o-anisidide	1.0	1.6	30	91.9	1.5	2.5	fused	57.5
9. Ethanesulfo-p-anisidide	1.0	0.75	25	63.6	0.8	2.2	fused	34.2
10. Ethanesulfo-o-anisidide	1.0	0.75	25	80.9	1.0	2.4	fused	46.2
11. Butanesulfo-p-anisidide	1.0	0.7	25	72.7	1.0	1.7	fused	15.1

SUMMARY

The bromination of some N-arylamides of alkanesulfonic acids with bromine and dioxane dibromide has been studied.

It has been shown that bromination by both methods forms the same products (monobromo derivatives of the anilides and toluidides and dibromo derivatives of the anisidides), but with better yields by direct bromination.

LITERATURE CITED

[1] A. G. Kostsova, N. M. Yanova, and Z. N. Sushko, J. Gen. Chem. 26, 2855 (1956);* A. G. Kostsova and N. T. Borisova, J. Gen. Chem. 28, 2420 (1958);* A. G. Kostsova, J. Gen. Chem. 28, 1573 (1958).*

[2] L. A. Yanovskaya, A. P. Terent'ev, and L. I. Belen'kii, J. Gen. Chem. 22, 1596 (1952).*

* Original Russian pagination. See C. B. translation.   Received November 12, 1958

SYNTHESIS OF N-ARYL-2,4-DIMETHYLQUINOLINIUM SALTS
AND THEIR DERIVATIVES

B. A. Tertov and B. I. Ardashev

Rostov-on-Don State University

Over recent years a number of papers have been published on the synthesis and study of the properties of quaternary salts from quinoline, quinaldine, lepidine, and their derivatives, with aryl radicals at the nitrogen atom [1-8]. However, up to the present nobody has synthesized N-aryl quaternary salts of quinoline bases containing alkyl groups in positions 2 and 4, which, in particular, may be of interest for the synthesis of certain cyanine dyes.

Continuing previous investigations [7, 8], we established that secondary aromatic amines condense with acetaldehyde and acetone in the presence of hydrochloric acid and nitrobenzene to form N-aryl-2, 4-dimethyl-quinolinium salts and their derivatives.
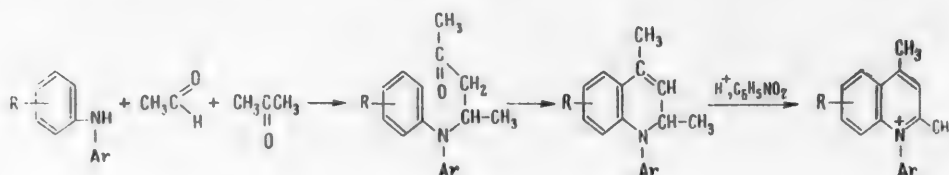
A large excess of acetone was used in the reaction so as to avoid the side formation of N-arylquinaldinium salts from diarylamines and acetaldehyde.

EXPERIMENTAL

N-Phenyl-2, 4-dimethylquinolinium perchlorate. Into a round-bottomed flask with a reflux condenser and a dropping funnel were placed 20 ml of acetone, 30 ml of alcohol, 15 ml of concentrated hydrochloric acid, and 30 ml of nitrobenzene. The contents of the flask were heated to boiling and from the dropping funnel was added a mixture of 10 g of diphenylamine, 2.7 ml of paraldehyde, and 17.3 ml of acetone over a period of 3 hours. When all the diphenylamine and paraldehyde had been added, the mixture was boiled for 1 hour. The reaction mixture was then diluted with 150 ml of water and steam distilled; the alcohol, acetone, and nitrobenzene were thus removed. The aqueous solution of N-phenyl-2,4-dimethylquinolinium chloride remaining in the flask was decanted from the tar, evaporated to a volume of 40-50 ml, boiled with activated charcoal, filtered free from the latter, and treated with a 5 % solution of perchloric acid. The precipitated crystals of N-phenyl-2,4-dimethylquinolinium perchlorate were collected and recrystallized from alcohol. We obtained 3 g (15 %) of a product which decomposed at 220-225°.

Found %: N 4.31; Cl 10.73. $C_{17}H_{16}O_4NCl$. Calculated %: N 4.19; Cl 10.62.

N-(2,4-Dimethylphenyl)-2,4,6,8-tetramethylquinolinium perchlorate. The synthesis was similar to the previous one. From 10 g of 2,2',4 ,4'-tetramethyldiphenylamine and 2 ml of paraldehyde we obtained 3.12 g (18 %) of product with m.p. 192°.

Found %: N 3.82; Cl 9.28. $C_{21}H_{24}O_4NCl$. Calculated %: N 3.59; Cl 9.09.

N-Phenyl-2,4-dimethyl-5,6-benzoquinolinium perchlorate. Into a round-bottomed flask fitted with a reflux condenser and a dropping funnel were placed 10 ml of acetone, 15 ml of concentrated hydrochloric acid, and 15 ml of nitrobenzene. The reaction mixture was heated to boiling and from the dropping funnel was added a solution of 5 g of N-phenyl-β-naphthylamine in a mixture of 10 ml of alcohol, 15 ml of acetone, and 1 ml of paraldehyde over a period of 1 hour. After this the reaction mixture was boiled for a further 3 hours. The quaternary salts were isolated as in previous experiments. Recrystallization from 50 % alcohol yielded 1.1 g (12.5 %) of a product with m.p. 209°.

Found %: Cl 9.43 . $C_{21}H_{18}O_4NCl$. Calculated %: Cl 9.21 .

N-(β-Naphthyl)-2,4-dimethyl-5,6-benzoquinolinium perchlorate was synthesized in the same way. From 4 g of β,β-dinaphthylamine and 0.7 ml of paraldehyde we obtained 1.2 g (18.5 %) of crystals with m.p. 199°.

Found %: Cl 8.41 . $C_{25}H_{20}O_4NCl$. Calculated %: Cl 8.17 .

SUMMARY

1. It was established that diarylamines condense with acetaldehyde and acetone in hydrochloric acid in the presence of nitrobenzene to form N-aryl-2,4-dimethylquinolinium salts and their derivatives.

2. Four compounds which have not been described in the literature were obtained.

LITERATURE CITED

[1] Heterocyclic Compounds [Russian translation] (Foreign Lit. Press, Moscow, 1955) vol. 4, p. 168 .

[2] G. T. Pilyugin and Z. Ya. Krainer, Doklady Akad. Nauk SSSR 81, 609 (1951) .

[3] G. T. Pilyugin, Izvest. Akad Nauk SSSR, Otdel. Khim. Nauk, 353 (1952).*

[4] G. T. Pilyugin and E. P. Opanasenko, Zhur. Obshchei Khim. 27, 1015 (1957).*

[5] G. Pilyugin and S.V. Shinkorenko, .C. A. 51, 2882 (1957).

[6] G. T. Pilyugin and S. V. Shinkorenko, Zhur. Obshchei Khim. 28, 1313, 1320 (1958).*

[7] B. I. Ardashev and B. A. Tertov, Zhur. Obshchei Khim. 29, 3050 (1959).*

[8] B. A. Tertov and V. I. Ardashev, Zhur. Obschei Khim. 27, 3026 (1957).*

* Original Russian pagination. See C. B. translation.

METHACRYLATION OF SOME AMINO ACIDS
AND THEIR DERIVATIVES

D. V. Ioffe and S. G. Kuznetsov
All-Union Scientific Research Institute of Health Chemistry

In recent years, in addition to esters of acrylic and methacrylic acids, the amides of these acids have attracted some attention as starting materials for the synthesis of polymers. Amides of acrylic and methacrylic acids substituted at the nitrogen are of considerable interest [1, 2]. Substituted methacrylamides are obtained either from amides of saturated acids [3] or from derivatives of methacrylic acid and appropriate amines. In the literature there are descriptions of two methods of synthesizing methacrylamides from methacrylic acid derivatives. One of these consistsof reacting methyl methacrylate with anilinomagnesium bromide or analogous organomagnesium compounds [4]. A more convenient method is the interaction of methacrylyl choride with an amine in an inert solvent (benzene or ether) [5-8]; excess of the amine acylated or some tertiary amine (dimethyl-aniline or triethylamine) is used to bind the hydrogen chloride liberated in the reaction zone. Methacrylyl chloride also reacts with amines in an aqueous medium [8, 9]. The N-substituted acrylamides obtained by any of these methods are usually readily polymerizable compounds.

The purpose of the present work was the methacrylation of aliphatic amino acids and their derivatives, namely, esters and dipeptides. It should be noted that while methacrylated aromatic amino acids and their esters have been obtained [6], methacrylated amino acids of the aliphatic series and their derivatives are unknown. Of analogous compounds, the literature contains descriptions of only bromoacrylglycylglycine [10] and ethyl esters of acrylglycine and acrylglycylglycine [11], which were obtained, however, not by direct acylation,but by other methods.

Amino acids are known to be acylated either in anhydrous or aqueous alkaline media, i.e., under conditions where the amino group is in the amine form. Our attempts to acylate glycine in dry benzene did not give a positive result and therefore we turned to the acylation of amino acids in an aqueous medium with a 2-fold excess of sodium hydroxide. The second equivalent of alkali, added gradually during the reaction, bound the hydrogen chloride liberated. At the end of the reaction, the reaction mixture was acidified and the precipitated product separated. Methacrylyl chloride was reacted with dipeptides similarly. Methacrylyl chloride was reacted with ethyl esters of glycine, phenylalanine, and glycylglycine in an inert solvent in the presence of triethylamine. To exclude possible polymerization of the reaction products, a small amount of hydroquinone was added to the reaction mixture.

The compounds obtained were solids (with the exception of the ethyl ester of methacrylglycine). The properties of the compounds obtained and also analysis results are given in the table.

The methacylated amino acids and their derivatives polymerized in the presence of benzoyl peroxide to form solid polymers. The ethyl esters of methacrylated amino acids polymerized especially readily. The polymers thus formed lost the alcohol group when treated with alkali and formed alkali-soluble polymers of methacrylated amino acids. Copolymerization of the ethyl ester of methacrylglycine with the dimethacryl ester of ethylene glycol gave a solid polymer, which, after hydrolysis, formed a cation-exchange resin. containing glycine in its structure. Similar cation-exchange resins containing phenyl-alanine and glycylglycine were obtained from the ethyl esters of methacrylphenylalanine and methacrylglycylglycine, respectively. Such resins may be of some interest due to the presence of amino acids and carbamide groups in their structure. In particular, such resins have a high swelling capacity (relative swelling capacity of up to 300%). It may be assumed that they will have a high capacity for large organic ions.

N-Substituted methacrylamides

Sample no.	Name of compound	Yield (in %)	Melting point	Recrystallization solvent	M* found	calc.	Nitrogen content (in %) found	calc.
1	Methacrylglycine	58	104°	Acetone + ether	141.3, 142.5	143.1	9.66, 10.02	9 79
2	Methacrylphenyl-alanine	60	99—100	Benzene	231.4, 234.2	233.3	6.22, 6.24	6.01
3	Methacrylglycyl-glycine	75	200—201	Water	204.0, 203.4	200.2	14.14, 14.16	13.99
4	Methacrylglycyl-phenylalanine	62	128	Acetone	292.4, 291.3	290.3	9.68, 9.78	9.65
5	Methacrylphenyl-alanylglycine	68	174	Benzene	292.4, 291.7	290.3	9.54, 9.57	9.65
6	Ethyl ester of ** methacrylphenyl	71	—	—	173.0, 170.2	171.2	8.22, 8.06	8.18
7	Ethyl ester of meth-acrylphenylalanine	64	56	Ether	263.2, 262.0	261.3	5.25, 5.32	5.36
8	Ethyl ester of meth-acrylglycylglycine	66	73—74	Benzene	226.4, 228.0	228.3	12.15, 12.33	12.27

* The molecular weights of compounds 1-5 were found by alkalimetric titration, and those of compounds 1-8, by bromometric titration.

** B.p. 134-135° (9 mm), n_D^{20} 1.4749, d_4^{20} 1.0816, MR_D 44.56; calc. 44.20.

EXPERIMENTAL

I. Methacrylation of amino acids and dipeptides. To a solution of 0.05 mole of amino acid or dipeptide in 25 ml of 2 N sodium hydroxide was added a small amount of hydroquinone (20-30 mg), the solution cooled to 0° and 0.05 mole (5.2 g) of methacrylyl chloride and 25 ml of 2 N sodium hydroxide added alternately with vigorous stirring. The temperature of the reaction mixture was kept at 0-2° during the reaction. During the whole time the reaction medium was alkaline to phenolphthalein. When the reagents had been added, the reaction mixture was acidified with a stream of hydrogen chloride with cooling. The precipitated product was separated and recrystallized.

2. Methacrylation of ethyl esters of amino acids. To a solution of 0.05 mole of the ethyl ester of the amino acid and 0.05 mole (5.0 g) of triethylamine in dry ether was added 0.05 mole (5.2 g) of methacrylyl chloride with stirring. The temperature of the reaction mixture was kept at 0-5°. At the end of the reaction, the precipitated triethylamine hydrochloride was removed and washed with ether, and the combined ether solutions evaporated. The residue was vacuum distilled or recrystallized.

3. Methacrylation of the ethyl ester of glycylglycine. To a solution of 8.0 g (0.05 mole) of the ethyl ester of glycylglycine and 5.0 g (0.05 mole) of triethylamine in dry chloroform was added 5.2 g (0.05 mole) of methacrylyl chloride with stirring. The temperature of the reaction mixture was kept at 0-5°. At the end of the reaction the chloroform was removed under reduced pressure, the residue treated with 50 ml of benzene, the precipitate removed, and the benzene evaporated to the beginning of crystallization.

4. Polymerization. The polymerization was carried out in block, in the presence of benzoyl peroxide (0.1-0.3 %) at 75-80° for the ethyl esters and at temperatures above the melting point for the other substances. The polymerization products were pale yellow solids.

5. Preparation of cation-exchange resin containing glycine. To 6 g of the ethyl ester of methacrylglycine was added 1 g of the dimethacryl ester of ethylene glycol, and 70 mg of benzoyl peroxide. The mixture was placed in an ampoule and the sealed ampoule heated for 24 hours at 75-80°. The solid polymer was removed from the ampoule and pulverized. The grains obtained were treated with 100 ml of 2 N sodium hydroxide for 3 hours at room temperature, the mass acidified, the resin separated, washed with water, and dried. Light-yellow

grains of resin were obtained. The relative swelling capacity of the H-form was 200 % and that of the Na-form, 340 %. The capacity of the resin for sodium ions, determined by titration [12], was 5.6 mg-equiv /g .

Resins containing phenylalanine and glycylglycine were prepared analogously. In the preparation of the resin containing phenylalanine, the hydrolysis with alkali was carrried out at 90-95° .

SUMMARY

1. A method was proposed for acylating amino acids and dipeptides with methacrylyl chloride in an aqueous alkaline medium.

2. Eight N-substituted methacrylamides which have not been described in the literature were prepared.

3. Polymerization of some N-substituted methacrylamides yielded cation-exchange resins containing amino acids.

LITERATURE CITED

[1] U.S. Pat. 2820772 ; C. A. 52, 6848 (1958).

[2] Canadian Pat. 519390 ; Ref. Zhur. Khim. 2, 6431 (1952).

[3] P. Bieber, Ann. de Chim. 9, 674 (1954).

[4] P. Bieber, Bull. Soc. Chim. 56, (1954).

[5] S. Patai, M. Bentov, and M. Reichman, J. Am. Chem. Soc. 74, 845 (1952).

[6] M. M. Koton, T. A. Sokolova, and G. M. Chetyrkina, Zhur. Obschei Khim. 27, 185 (1957).

[7] T. A. Sokolova, Zhur. Obshchei Khim. 27, 2205 (1957).

[8] M. M. Koton, T. A. Sokolova, M. N. Savitskaya and T. M. Kiseleva, Zhur. Obshchei Khim. 27, 2239 (1957).

[9] T. A. Sokolova and L. A. Ovsyannikova, Zhur. Obshchei Khim. 28, 779 (1958).

[10] E. Fischer, Ber. 37, 2511 (1904).

[11] D. A. Smith and C. C. Unruh, J. Org. Ch. 23, 301 (1958).

[12] A. A. Vansheidt, A. A. Vasil'ev, and O. I. Okhrimenko, Coll. Theory and Practice of the Application of Ion-Exchange Materials [in Russian](1955) p. 110 .

• Original Russian pagination. See C. B. translation.

CYANINE DYES WITH UNSATURATED SUBSTITUENTS

VI. MONOMETHYNECYANINES AND STYRIL DYES CONTAINING STYRYL AND γ-PHENYLBUTADIENYL RADICALS IN THE BENZTHIAZOLE NUCLEI

I. K. Ushenko and S. E. Gornostaeva

Institute of Organic Chemistry, Academy of Sciences Ukrainian SSR

In previous communications [1-5] we described different cyanine dyes containing unsaturated substituents in the heterocyclic nuclei. Monomethynecyanines and styril dyes with unsaturated grouping remained unknown. In the present work we describe the synthesis of dyes of this type. It could have been expected that due to conjugation of the unsaturated groupings with the polymethyne chromophore of the monomethynecyanine or styril, the conjugation chain must increase, and as a result the color of the dye must deepen. This hypothesis was completely confirmed.

The starting bases were obtained by the reaction of benzthiazolyldiazonium chlorides with cinnamic acid or its derivatives under the conditions of the Meerwein reaction [6]. We had previously prepared 2-methyl-6-styrylbenzthiazole, 2-methyl-6-p-methoxystyrylbenzthiazole, 2-methyl-6-(α-thienylvinyl)-benzthiazole, and their quaternary salts [1]. Below we give the synthesis of some new bases, obtained by reaction of diazotized 2-methylmercapto-6-aminobenzthiazole with cinnamic, p-methoxycinnamic, and styrylacrylic acids. The bases obtained are listed in Table 1.

The data in Table 1 show that the yield of bases containing unsaturated substituents is low, as we also observed previously [1, 2]. The low yield of the bases is caused by a number of side processes : the formation of Sandmeyer reaction products, azo resins, and also oily substances, whose structure has not yet been established. The bases listed readily formed quaternary salts when treated with alkylating agents.

For the preparation of monomethynecyanines, the quaternary salts containing an active methyl group were condensed with quaternary salts of 2-methylmercaptobenzthiazoles in anhydrous alcohol in the presence of triethylamine.
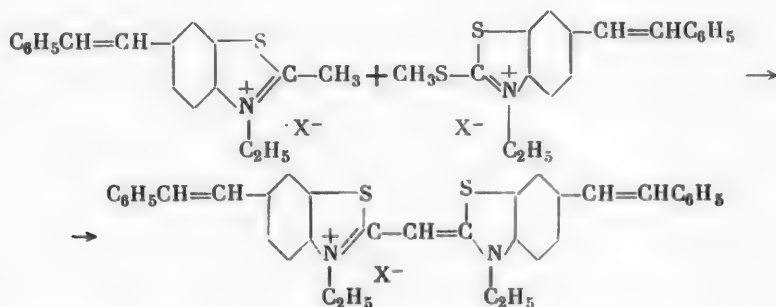
Table 2 gives some monomethynecyanines containing unsaturated substituents in the benzthiazole nuclei.

TABLE 1

Bases
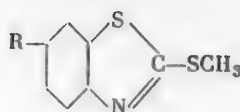
Compound No.	R	Yield (in %)
I	$C_6H_5CH=CH$	7.8
II	$p-CH_3OC_6H_4CH=CH$	9.3
III	$C_6H_5(CH=CH)_2$	17.4

The data in Table 2 show that in all cases the introduction of unsaturated substituents into the monomethynecyanine molecule produced a strong bathochromic effect, equal to 60 mμ. Styryl and γ-phenylbutadienyl substituents produced a bathochromic effect which was stronger than that of many auxochromic groups, and on the same level as that of the the dimethylamino group [7-9].

Quaternary salts containing unsaturated substituents in the benzthiazole nucleus were also condensed with p-dimethylaminobenzaldehyde. The absorption maxima of the styril dyes synthesized are given in Table 3.

The introduction of unsaturated groupings into position 6 of the styril dyes also produced a considerable shift in the absorption maximum into the long-wave part of the spectrum, which reached 28 mμ.

EXPERIMENTAL

2-Methylmercapto-6-aminobenzthiazole was obtained by reduction of 2-methylmercapto-6-nitrobenzthiazole [10] with stannous chloride in hydrochloric acid. The small tablets, from alcohol, had m.p. 110-111°.

2-Methylmercapto-6-styrylbenzthiazole (I). 19.6 g of 2-methylmercapto-6-aminobenzthiazole was dissolved in 70 ml of hot concentrated hydrochloric acid and 58 ml of water, the solution cooled to -5°, and the substance diazotized with 7.5 g of sodium nitrite in 16 ml of water. Into a three-necked flask fitted with a thermometer and a mercury seal and connected to a Tishchenko bottle with a barium hydroxide solution were placed 14.8 g of cinnamic acid, 67.2 g of sodium acetate, 400 ml of acetone, and 5.1 g of curpic chloride $(CuCl_2 \cdot 2H_2O)$ in 10 ml of water. The mixture was cooled to -5° and the diazonium chloride solution added with vigorous stirring over a period of 10-15 minutes. Stirring was then continued for 4 hours while the temperature of the reaction mixture gradually rose to room temperature. On the following day the mixture was heated to 50-55° and stirred for a further half an hour. When the mixture had cooled, the precipitate was collected, washed with acetone, and the aqueous acetone filtrate steam distilled. Distillate was collected until halogen was absent from the last portions. 1.9 g of 2-methylmercapto-6-chlorobenzthiazole was isolated from the distillate. When the contents of the distillation flask were cooled, the aqueous solution deposited 4.9 g of cinnamic acid. The dark, viscous mass remaining in the flask was dissolved in 300 ml of chloroform and the solution washed with 12% ammonia to remove the acid products, and then with water until neutral. The solution was dried with calcium chloride, reduced to a volume of 70-80 ml, and chromatographed on aluminum oxide. Chloroform was used for elution. The first, light-yellow zone was collected separately; the more impure eluate was rechromatographed. Removal of the chloroform from the combined eluated yielded 5.5 g of an oily yellow product. Two recrystallizations from isopropyl alcohol gave 2.2 g (7.8 %) of base. The yield on the cinnamic acid reacting was 10.6 %. The light-yellow platelets had m.p. 104-105°.

Found %: N 5.12, 5.16; S 22.86, 23.06. $C_{16}H_{13}NS_2$. Calculated %: N 4.95; S 22.62.

2-Methylmercapto-6-(p-methoxystyryl)-benzthiazole (II). 19.6 g of 2-methylmercapto-6-aminobenzthiazole was diazotized as described above. Over a period of 1 hour the benzthiazolyldiazonium chloride solution was introduced into a reactor containing 16.8 g of p-methoxycinnamic acid, 67.2 g of sodium acetate, 400 ml of acetone, and a solution of 5.1 g of cupric chloride in 10 ml of water. The reaction mixture was stirred for 8 hours while the temperature slowly rose from -10° to +22°. On the following day the mixture was heated to 50° and stirred for 1 hour (until the evolution of carbon dioxide ceased completely). The base was isolated and purified as described above. Recrystallization from isobutyl alcohol with animal charcoal gave 2.6 g of base. The colorless scales had m.p. 151-152°.

Found %: N 4.57, 4.62; S 20.70. $C_{17}H_{15}ONS_2$. Calculated %: N 4.47; S 20.45.

2-Methylmercapto-6-(4'-phenylbutadienyl-1')-benzthiazole (III). 19.6 g of 2-methylmercapto-6-amino-benzthiazole was diazotized as described above. Into a flask were placed 17.4 g of styrylacrylic acid, 400 ml of

TABLE 2

Monomethynecyanines

R—[benzothiazole]—S / C—CH=C \ S—[benzothiazole]—R'
with N⁺—C_2H_5 and N—C_2H_5, X⁻
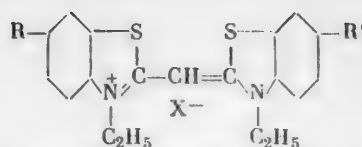
Compound No.	R	R'	Absorption maximum (in mμ)	Shift in absorp-maximum (in mμ)
—	H	H	422	—
IV	$C_6H_5CH=CH$	$C_6H_5CH=CH$	466	+44
V	p-$CH_3O—C_6H_4CH=CH$	$C_6H_5CH=CH$	468	+46
VI	[thiophene]—$CH=CH$	$C_6H_5CH=CH$	469	+47
VII	p-$CH_3OC_6H_4CH=CH$	p-$CH_3OC_6H_4CH=CH$	474	+52
VIII	[thiophene]—$CH=CH$	p-$CH_3OC_6H_4CH=CH$	474	+52
IX	$C_6H_5(CH=CH)_2$	$C_6H_5(CH=CH)_2$	482	+60
X	H	$C_6H_5CH=CH$	446	+24
XI	H	p-$CH_3OC_6H_4CH=CH$	450	+28
XII	H	[thiophene]—$CH=CH$	451	+29

TABLE 3

Styril Dyes

·R—[benzothiazole]—S / C—CH=CH—[phenyl]—$N(CH_3)_2$ with N⁺—C_2H_5, X⁻
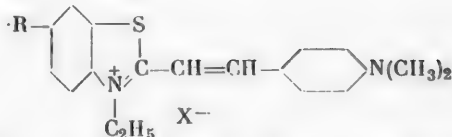
Compound No.	R	Absorption maximum (in mμ)	Shift in absorption maximum (in mμ)
---	H	530	—
XVII	$C_6H_5CH=CH$	548	+18
XVIII	p-$CH_3OC_6H_4CH=CH$	552	+22
XIX	[thiophene]—$CH=CH$	555	+25
XX	$C_6H_5(CH=CH)_2$	558	+28

acetone, 67.2 g of sodium acetate, and 5.1 g of cupric chloride and 10 ml of water. The mixture was cooled to -10° and the cooled diazonium solution added to it over a period of 10 minutes. Stirring was continued for 5 hours while the temperature of the reaction mixture gradually rose to room temperature. On the following day the mixture was stirred at 20° for 3 hours and at 50-55° for half an hour. The evolution of carbon dioxide ceased only at the end of heating . After 20 mg of hydroquinone had been added to the reaction mixture, the latter was steam distilled. The contents of the flask were poured into a beaker, where the dark, viscous mass solidified on cooling. This was then separated, powdered, washed with water, dried, dissolved in chloroform, and the solution filtered and chromatographed on aluminum oxide. The chloroform was distilled from the eluate to leave a light yellow oil which crystallized on cooling. The weight was 10.8 g (34.8 %). To the precipitate was added 15 ml of methanol, the mixture stirred, and the precipitate collected and dried. The yield was 5.4 g and the m.p. 143-144°. The base did not contain halogen. After recrystallization from alcohol the product had m.p. 145-146°, which did not change further. The solutions and also the solid base fluoresced strongly in ultraviolet light.

Found % : S 20.80, 20.70 . $C_{18}H_{15}NS_2$. Calculated % : S 20.71 .

TABLE 4

Compound no.	Name of dye	Substituted quaternary salts (in g)		Recrystallization solvent	External appearance of dye	Yield (in %)	Melting point	Found		Calculated		
		2-methyl-benzthiazole	2-methyl-mercapto-benzthiazole					element	content (in %)	empirical formula	element	content (in %)
IV	3,3'-Diethyl-6,6'-distyryl-monomethynethiacyanine iodide	B, 0.45	A, 0.47	Nitromethane	Yellow crystals	43	248°	S	9.39, 9.48	$C_{35}H_{31}N_3S_2$	S	9.55
V	[3-Ethyl-6-(p-methoxystyryl)-benzthiazole-(2)]-[3'-ethyl-6'-styrylbenzthiazole-(2')]-monomethynethiacyanine iodide	C, 0.48	A, 0.47	The same	Light brown crystals	32	196	S	9.60, 9.80	$C_{36}H_{33}ON_3S_2$	S	9.15
VI	[3-Ethyl-6-(α-thienylvinyl)-benzthiazole-(2)]-[3'-ethyl-6'-styrylbenzthiazole-(2')]-monomethynecyanine iodide	D, 0.46	A, 0.47	Formamide	Golden brown crystals	33	257	S	13.70	$C_{33}H_{29}N_2S_3I$	S	14.20
VII	3,3'-Diethyl-6,6'-di-p-methoxystyryl-monomethynethiacyanine iodide	C, 0.24	E, 0.25	Mixture of pyridine and methanol (1:1)	Yellow-orange crystals	30	255	I	17.28, 17.13	$C_{37}H_{35}O_2N_2S_2I$	I	17.40
VIII	[3-Ethyl-6-(α-thienylvinyl)-benzthiazole-(2)]-[3'-ethyl-6'-(p-methoxystyryl)-benzthiazole-(2')]-monomethyne-cyanine iodide	D, 0.23	E, 0.25	The same (1:2)	Orange-yellow crystals	45	242	S	13.39, 13.57	$C_{34}H_{31}ON_2S_3I$	S	13.50
IX	3,3'-Diethyl-6,6'-di-(4'-phenylbutadienyl-1')-monomethynecyanine iodide	I, 0.47	I, 0.4	Pyridine—methanol (1:2), then from ethyl alcohol	Fine, yellow-orange crystals	27	212-213 (decomp.)	I	17.20, 17.22	$C_{39}H_{35}N_2S_2I$	I	17.59
X	[3-Ethyl-benzthiazóle-(2)]-[3'-ethyl-6'-styrylbenzthiazole-(2')]-monomethyne cyanine iodide	B, 0.45	F, 0.34	Formamide	Light yellow crystals	31	172-173	S	11.38, 11.50	$C_{27}H_{24}N_2S_2I$	S	11.29

Compound no.	Name of dye	Substituted quaternary salts (in g)		Recrystallization solvent	External appearance of dye	Yield (in %)	Melting point	Found		Calculated		
		2-methyl-benzthiazole	2-methyl-mercapto-benzthiazole					element	content (in %)	empirical formula	element	content (in %)
XI	[3-Ethylbenzthiazole-(2)]-[3'-ethyl-6'-(p-methoxystyryl)-benzthiazole-(2')]-monomethynecyanine iodide	C, 0.24	F, 0.17	The same	The same	53	234°	S	10.64, 10.70	$C_{29}H_{26}ON_4S_2I$	S	10.72
XII	[2-Ethylbenzthiazole-(2)]-[3'-ethyl-6-(α-thienyl-vinyl)-benzthiazole-(2')]-monomethynecyanine iodide	D, 0.23	F, 0.17	Nitro-methane	Yellow crystals	36	278	S	16.61, 16.62	$C_{25}H_{23}N_3S_3I$	S	16.76
XIII	[3'-Ethyl-6,7-benzothiazole-(2)]-[3'-ethyl-6-(p-methoxystyryl)-benzthiazole-(2')]-monomethynecyanine p-toluenesulfonate	C, 0.96	G, 0.88	Alcohol	Yellow orange tablets	36	275-276	S	13.81, 13.65	$C_{36}H_{36}O_4N_2S_3$		13.87
XIV	[3-Ethyl-6-styrylbenzthiazole-(2)]-[3-ethyl-4-phenylthiazole-(2')]-monomethyne-cyanine iodide	B, 0.45	H, 0.41	The same	Yellow crystals	20	239	S	10.80, 10.94	$C_{29}H_{27}N_3S_2I$	S	10.77
XV	[3-Ethyl-6-(p-methoxystyryl)-benzthiazole-(2)]-[3'-ethyl-4'-phenylthiazole-(2')]-monomethynecyanine iodide	C, 0.48	H, 0.41	"	Greenish yellow crystals	40	243	S	10.33, 10.58	$C_{30}H_{29}ON_2S_2I$	S	10.26
XVI	[3-Ethyl-6-(α-thienylvinyl)-benzthiazole-(2)]-[3'-ethyl-4'-phenylthiazole-(2')]-monomethynecyanine iodide	D, 0.46	H, 0.41	"	Light green needles	25	251	S	15.52, 15.46	$C_{27}H_{25}N_3S_3I$	S	16.00

Ethylbenzenesulfonate of 2-methylmercapto-6-styrylbenzthiazole. 0.85 g of 2-methylmercapto-6-styryl-benzthiazole and 0.94 g of ethyl benzenesulfonate were heated on an oil bath at 140-150° for 6 hours. The salt was dissolved in boiling water and the solution decolorized with animal charcoal and evaporated on a water bath. The yield was 1.3 g (92 %). The product was used without further purification.

Ethylbenzensulfonate of 2-methylmercapto-6-(p-methoxystyryl)-benzthiazole. 0.93 g of 2-methylmercapto-6-(p-methoxystyryl)-benzthiazole and 0.94 g of ethyl benzensulfonate were heated at 150-160° for 8 hours. The yield was 1 g (74 %). The light-yellow powder had m.p. 162-163°. The product was used without further purification.

Ethyl-p-toluenesulfonates of 2-methyl-6-styrylbenzthiazole, 2-methyl-6-(p-methoxystyryl)-benzthiazole, 2-methyl-6-(α-thienylvinyl)-benzthiazole, and 2-methyl-6-(4'-phenylbutadienyl-1')-benzthiazole were described by us previously [1, 3].

2-Methylmercapto-4-phenylthiazole was obtained from methyl dithiocarbamate [11] and bromoacetophenone [12].

Ethyl-p-toluenesulfonate of 2-methylmercapto-4-phenylthiazole. To 1.8 g of 2-methylmercapto-4-phenyl-thiazole was added 2 g of ethyl p-toluenesulfonate. The mixture was heated at 135-145° for 5 hours. The usual processing yielded 2 g (56 %) of quaternary salt as a brownish viscous oil. The salt was used without further purification.

The ethyl-p-toluenesulfonate of 2-methylmercapto-6, 7-benzobenzthiazole was obtained by us previously [13].

Synthesis of dyes. A general procedure was used for synthesizing the monomethynecyanines. The quaternary salt of the substituted benzthiazole, containing an active methyl group in position 2, was dissolved in 10-20 ml of anhydrous alcohol. To the solution was added the second component, namely, the quaternary salt of 2-methyl mercaptobenzthiazole and 0.5 ml of triethylamine. The mixture was boiled for 20-30 minutes, the dye precipitated with a hot aqueous solution of potassium iodide, and the precipitate collected, washed with warm water, methanol, and ether, and recrystallized 2-3 times from an appropriate solvent. Table 4 gives the conditions of synthesizing the monomethynecyanines and the analysis results. The following symbols were used for the starting quaternary salts : ethylbenzenesulfonate of 2-methylmercapto-6-styrylbenzthiazole (A), ethyl-p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole (B), ethyl-p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole (C), ethyl -p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole (D), ethylbenzenesulfonate of 2-methylmercapto-6-(p-methoxystyryl)-benzthiazole (E), iodoethylate of 2-methylmercaptobenzthiazole (F), ethyl-p-toluenesulfonate of 2-methylmercapto-6, 7-benzobenzthiazole (G), ethyl-p-toluenesulfonate of 2-methylmercapto-4-phenylthiazole (H), ethyl-p-toluenesulfonate of 2-methyl-6-(4'-phenylbutadienyl-1')-benzthiazole (I), and ethyl-p-toluenesulfonate of 2-methylmercapto-6-(4'-phenylbutadienyl-1')-benzthiazole (J).

Iodoethylate of 2-(p-dimethylaminostyryl)-6-styrylbenzthiazole (XVII). A mixture of 0.5 g of the ethyl-p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 0.16 g of p-dimethylaminobenzaldehyde, and 4 ml of acetic anhydride was boiled for 25 minutes. The reaction mixture was poured into a hot solution of potassium iodide. The precipitate was collected, washed with water and a small amount of methanol, and successively recrystallized from isobutyl and ethyl alcohols. The yield was 0.23 g (40 %). The fine dark-green crystals had m.p. 223°.

Found % : N 5.00, 4.96 . $C_{27}H_{27}N_2SI$. Calculated % : N 5.20 .

The bromoethylate of 2-(p-dimethylaminostyryl)-6-(p-methoxystyryl)-benzthiazole (XVIII) was obtained analogously from 0.48 g of the ethyl-p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole and 0.3 g of p-dimethylaminobenzaldehyde. The yield was 0.23g(44 %). The dark-green crystals had m.p. 236°.

Found %: Br 15.47, 15.65. $C_{28}H_{29}ON_2SBr$. Calculated %: Br 15.35

The iodoethylate of 2-(p-dimethylaminostyryl)-6-(α-thienylvinyl)-benzthiazole (XIX) was obtained by boil-ing 0.46 g of the ethyl-p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole and 0.3 g of p-dimethyl-aminobenzaldehyde in 5 ml of acetic anhydride. When the product had been recrystallized twice from isomyl alco-hol, the yield was 0.15 g (27%). The dark green crystals had m. p. 224°.

Found %: N 5.18, 5.31 $C_{25}H_{25}N_2S_2I$. Calculated %: N 5.15.

Bromoethylate of 2-(p-dimethylaminostyryl)-6-(4'-phenylbutadienyl-1')-benzthiazole (XX). A mixture of 0.47 g of the ethyl-p-toluenesulfonate of 2-methyl-6-(4'-phenylbutadienyl-1')-benzthiazole, 0.15 g of dimethyl-

aminobenzaldehyde, and 6 ml of acetic anhydride was boiled for 30 minutes. The precipitate of dye was collected and recrystallized twice from alcohol. The yield was 0.16 g (31 %). The fine black crystals had m.p. 243°.

Found %: N 5.26, 5.22 . $C_{29}H_{23}N_2SBr$. Calculated %: N 5.41 .

SUMMARY

1. The interaction of diazotized 2-methylmercapto-6-aminobenzthiazole with cinnamic, p-methoxycinnamic, and styrylacrylic acids under the conditions of the Meerwein reaction yielded three new bases containing unsaturated substituents in position 6. When treated with alkylating agents, the bases were converted into quaternary salts.

2. Condensation of the quaternary salts, which have an active methyl group, with quaternary salts of 2-methyl-mercaptobenzthiazoles gave a number of monomethynecyanines containing unsaturated radicals in the benzthiazole nucleus.

3. It was established that the introduction of unsaturated radicals into positions 6,6' of monomethynecyanines produced a bathochromic effect of up to 60 mμ .

4. Some styril dyes containing unsaturated substituents in position 6 were synthesized. It was shown that the introduction of unsaturated substituents into position 6 of styril dyes produced a considerable shift in the absorption maximum into the long-wave region of the spectrum.

LITERATURE CITED

[1] I. K. Ushenko and S. E. Gornostaeva, Zhur. Obshchei Khim. 28, 1668 (1958).*

[2] M. A. Al'perovich, I. K. Ushenko, and L. N. Tyurina, Zhur. Obshchei Khim. 28, 2538 (1958).*

[3] M. A. Al'perovich, L. K. Ushenko, and L. N. Tyurina, Zhur. Obschei Khim. 29, 3376 (1959).*

[4] M. A. Al'perovich and L. K. Ushenko, Zhur. Obshchei Khim. 29, 3384 (1959). *

[5] M. A. Al'perovich, L. K. Ushenko, L. N. Tyurina, and M. K. Grechko, Zhur. Obshchei Khim. 29, 3606 (1959).*

[6] H. Meerwein, E. Büchner, and K. Emster, J. Pr. Ch. 152, 237 (1939) .

[7] A. I. Kiprianov, I. K. Ushenko, and E. D. Sych. Zhur. Obschei Khim. 15, 200 (1945).*

[8] A. I. Kiprianov and I. K. Ushenko, Zhur. Obshchei Khim. 15, 207 (1945).

[9] I. L. Levkoev, N. N. Sveshnikov, and S. A. Kheifits, Zhur. Obshchei Khim. 16, 1489 (1946).

[10] C. Hasan and R. Hunter, J. Chem. Soc. 1674 (1936).

[11] J. Braun, Ber. 35, 3380 (1902).

[12] E. Knott, J. Chem. Soc. 1658 (1947).

[13] I. K. Ushenko, Zhur. Obshchei Khim. Collection I, 521 (1953).

SOME INDOLE DERIVATIVES

E. E. Baroni and K. A. Kovyrzina

The simplest method of preparing aromatic derivatives of indole is that of Bischler [1, 2]. This method consists of reacting primary aromatic amines and their hydrochlorides with α-hydroxy and α-halo ketones. Practical aspects of the condensation were studied by Japp [3]. Contrary to the data of Voigt [11], who condensed benzoin with aromatic amines in a sealed tube, it was found that the synthesis could be achieved in an open beaker at 180-200° in 1-2 hours. The yield reached 50-75 %.
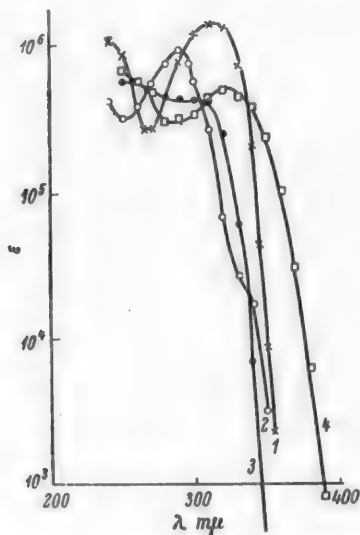
Fig. 1. Absorption spectra of indoles in alcohol (10^{-3} mole/liter). 1) 2-Phenyl-indole, 2) 1,2-diphenylindole, 3) 1,3-diphenylindole, 4) 2,3-diphenylindole.
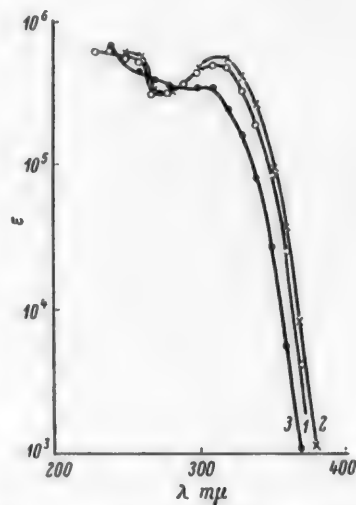
Fig. 2. Absorption spectra of indoles in alcohol (10^{-3} mole/liter). 1) 2,3-Diphenyl-7-methylindole, 2) 2,3-diphenyl-5-methyl-indole, 3) 2,3-diphenyl-1-methylindole.

By this method we obtained the following indole derivatives: 2,3-diphenyl-1-methyl-, 2,3-diphenyl-7-methyl-, 2,3-diphenyl-5-methyl-, and 2,3-diphenyl-β-naphthoindole.

The action of secondary aromatic amines on α-hydroxy, α-halo, and α-arylamino ketones has been studied little as yet. There is only the work of Richards [4], who reacted diphenylamine with benzoin and obtained 1,2,3-triphenylindole. We investigated the action of diphenylamine on α-halo ketones. It was established that the reaction of diphenylamine with α-halo ketones was not difficult to accomplish. The action of diphenylamine on ω-bromoacetophenone was used to synthesize a new disubstituted derivative, 1,3-diphenyl-indole. The absorption spectra of the indoles obtained are given in Figs. 1, 2, and 3.

A whole series of optical and chemical properties of complex cyclic molecules are known to be determined by the generalized electron cloud. The unshared electron pair of the nitrogen atom is capable of interacting with

TABLE 1

α-Hydroxy and α-halo ketones	Aromatic amines	Product	Method	Yield (%)	Literature
Benzoin	Aniline and its hydrochloride	2,3-Diphenylindole	I	67	[11, 3]
	o-Toluidine and its hydrochloride	2,3-Diphenyl-7-methylindole	I	75	[11, 3]
	p-Toluidine and its hydrochloride	2,3-Diphenyl-5-methylindole	I	68	[11, 3]
	α-Naphthylamine and its hydrochloride	2,3-Diphenyl-α-naphthoindole	I	57.5	[11, 3]
	β-Naphthylamine	2,3-Diphenyl-β-naphthoindole	II	53	[11, 3]
α-Bromodesoxybenzoin	Monomethylaniline	2,3-Diphenyl-1-methylindole	III	72	—
ω-Bromoacetophenone	Diphenylamine	1,3-Diphenylindole	I	35	—
Benzoin	Diphenylamine	1,2,3-Triphenylindole	I	—	[4]
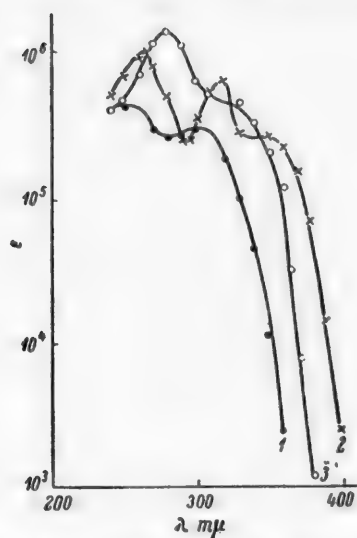
Fig. 3. Absorption spectra of indoles in alcohol (10^{-3} mole/liter). 1) 1,2,3-Triphenylindole, 2) 2,3-diphenyl-β-naphthoindole, 3) 2,3-diphenyl-α-naphthoindole.

π-electrons of a chain of conjugated bonds, and by being included in the general electron system of the molecule, substantially increases its polarizability. Due to this there is a rearrangement of the density of the electron cloud and the formation of an ionic state corresponding to formulas (I) and (II) becomes possible in the 1,3-diphenylindole molecule. In this connection, it is interesting to mention papers [5-7], where reports were given on the connection between fluorescence capacity and the structure of phenyl derivatives of Δ^2-pyrazoline, where the nitrogen atom plays a similar role.

All the indole compounds we obtained had a strong fluorescence in the ultraviolet region of the spectrum and could be incorporated into polystyrene without any particular difficulty to give high-grade plastic scintillators [8]. This required products of special purity, and therefore the indoles obtained were sublimed in high vacuum ($5 \cdot 10^{-4}$ mm Hg). Sublimation, and then recrystallization from n-heptane made it possible to obtain 1,2-diphenylindole in a crystalline form (it was previously described in the literature as an oil [2]).
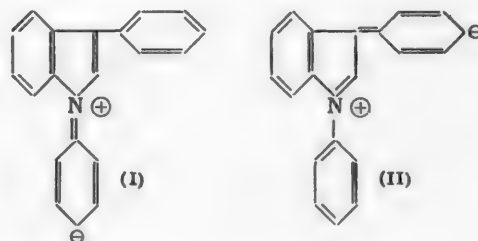
EXPERIMENTAL

Method I. 1 mole of α-hydroxy ketone, 3 moles of primary aromatic amine, and 1 mole of its hydrochloride were heated in an open beaker to 180-200° for 2 hours. The reaction mass was distributed between

TABLE 2

Name of indole	Boiling point (pressure in mm)	Melting point	n_g^{20} *	Molecular weight	
				found	calc.
2,3-Diphenylindole	260—270° (2)	123—124°	1.6391	269.55	269.33
2,3-Diphenyl-7-methylindole	270 (9) 238 (2)	135	1.6600	283.9	283.35
2,3-Diphenyl-5-methylindole	270—285 (10)	152—153	1.6691	284.8	283.35
2,3-Diphenyl-α-naphthoindole	280—285 (8) 330—340 (18)	140—141	1.6874	319.8	319.38
2,3-Diphenyl-β-naphthoindole	310 (8—6)	166—167	—	318.8	319.38
2,3-Diphenyl-1-methylindole	—	139	—	283.0	283.35
1,3-Diphenylindole	200—230 (3)	103—104	1.6524	271.1	269.33
1,2-Diphenylindole [9]	49	—	—	—	—
2-Phenylindole [10]	186	—	—	—	—
1,2,3-Triphenylindole [4]	185	—	—	—	—

* Refractive indices obtained by calculation from the refractive indices of a 10% solution in benzene.

ether and dilute hydrochloric acid. The ether layer was dried, the ether removed, and the residue vacuum distilled to give a weakly colored oil which rapidly solidified. Treatment with n-heptane and prolonged standing (3-6 days) yielded fine crystals. The product was purified by recrystallization from alcohol.

Method II . 1 mole of benzoin, 3 moles of β-naphthylamine, and 1.5 mole of zinc chloride were boiled for 10 minutes in an open beaker.

Method III. 1 mole of α-halo ketone and 3 moles of monomethylaniline were heated. The preparation of 1,3-diphenylindole required a mixture of 1 mole of ω-bromoacetophenone, 3.5 moles of diphenylamine, and 5-6 drops of pyridine.

The indole syntheses are given in Table 1. Table 2 gives some physical data.

SUMMARY

Methods reported in the literature for preparing phenyl derivatives of indole by Bishler's method were refined and 1,2-diphenylindole was isolated in a pure form.

1,3-Diphenylindole, which has not been described until now, was synthesized and the absorption spectra of the compounds described are presented.

LITERATURE CITED

[1] Bischler, Brion, Ber. 25, 2860 (1892).

[2] Bischler, Fireman, Ber. 26, 1336 (1893).

[3] J. R. Japp and T. S. Murray, Ber. 26, 2638 (1893).

[4] M. B. Richards, J. Chem. Soc. 97, 977 (1910).

[5] E A. Andreeshchev, E. E. Baroni, and K. A. Kovyrzina. Report to the 2nd Scientific Coordination Conference on the Synthesis, Production, and Application of Scintillators [in Russian], Khar'kov, September 27-30, 1957.

[6] O. Neunhoeffer and H. Ulrich, Ber. 88, 1123 (1955); D. Rosahl, Ann. Phys. 12, 35 (1953); O. Neunhoeffer and D. Rosahl, Z. Elektrochem. 57, 81 (1953).

[7] R. H. Wiley, C H. Jarboe, F. N. Hayes, E. Hansbury, J. T. Nielsen, P. X. Callahan, and M. C. Sellars, J. Org. Ch. 23, 732 (1958).

[8] E. A. Andreeshchev, E. E. Baroni, K. A. Kovyrzina, L. É. Pani, I. M. Rozman, and V. M. Shoniya, Prib. i Tekhn. Éksper. 1, 32 (1956); E. A. Andreeshchev, E. E. Baroni, K. A. Kovyrzina, I. M. Rozman, and V. M. Shoniya, Izvest. Akad. Nauk SSSR, Otdel. Fiz. Nauk. 22, 67 (1958).

[9] Pfüle, Ann. Chem. 239, 223 (1887).

[10] E. Fischer, Ann. Chem. 236, 133 (1886).

[11] E Voigt, J. pr. Ch. (2), 31, 544; 34, 2 (1893).

SYNTHESIS OF 2-[DI-(β-CHLOROETHYL)-AMINO]-4-(2,6,6-TRIMETHYL CYCLOHEXENYL)-BUTANE

A. Ya. Berlin and N. G. Chernova

Institute of Experimental Pathology and Cancer Therapy,
Academy of Medical Sciences USSR

Among effective chemotherapeutic agents with an antitumor action, one of the most important positions is occupied by very diverse derivatives of bis-(β-chloroethyl)-amine. The most valuable substances in this respect are apparently those which contain residues of natural amino acids [1] and heterocycles [2].

It seemed interesting to us to study bis-β-chloroethylamine derivatives of substances which are similar in structure to groupings found in the vitamin A molecule. Some compounds of this type, for example, β-ionone and citral, are used in medicine and according to literature reports [3], the latter has an appreciable antitumor action.

In the present work we describe the synthesis of 2-[di-(β-chloroethyl)-amino]-4-(2,6,6-trimethylcyclohexenyl)-butane (IV), which is a derivative of dihydro-β-ionylamine. It is interesting that dihydro-β-ionylamine itself is a biologically active substance as it has a considerable spasmolytic activity [4].

Reductive amination of β-ionine (I) with Raney nickel by Haskelberg's method [5] gave dihydro-β-ionylamine (II); the proof of its structure was based on chemical analogies [4-6]. The latter condensed smoothly with ethylene oxide [7] to form 2-[di-(β-hydroxyethyl)-amino]-4-(2,6,6-trimethylcyclohexenyl)-butane (III).

The action of thionyl chloride on (III) in chloroform solution [8] gave the hydrochloride of 2-[di-(β-chloroethyl)-amino]-4-(2,6,6-trimethylcyclohexenyl)-butane (IV) in 66 % yield.

Biological investigation * showed that the hydrochloride of dihydro-β-ionylamine and the hydrochloride of N,N-di-(β-chloroethyl)-dihydro-β-ionylamine (IV) had no antitumor activity.

---
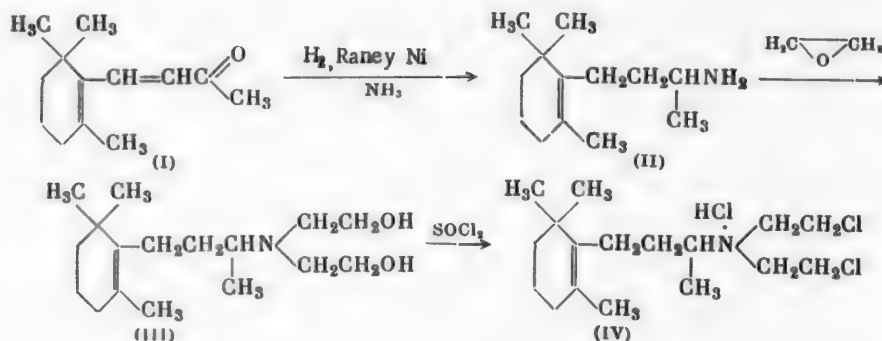
*Carried out in our institute.

EXPERIMENTAL

Dihydro- β -ionylamine (II). 15 g of β-ionone with b.p. 124-125.5° at 8.5 mm and n_D^{20} 1.5187 was dissolved in 45 ml of 96 % ethanol saturated with ammonia. The substance was hydrogenated in the presence of 6 g of Raney nickel at 50-55°. The mixture was shaken for 27 hours, when 3.15 liters of hydrogen was absorbed. At the end of the hydrogenation, the catalyst was removed by filtration and washed with alcohol, and the solvent distilled from the combined filtrates. The oily residue was distilled in a stream of nitrogen. We obtained 11.6 g (79.4 %) of a clear, slightly yellowish oil with b.p. 101.5-103.5° (5 mm), n_D^{21} 1.4839 .

After recrystallization from a mixture of benzene and ligroin, the hydrochloride of (II) had m.p. 215.5-216°. According to literature data [5], the m.p. is 212°.

2-[Di-(β-hydroxyethyl)-amino]-4-(2,6,6-trimethylcyclohexenyl)-butane (III). A mixture of 15 g of dihydro-β-ionylamine (II), 8.8 g of ethylene oxide, and 1 ml of water were left for 44 hours in a sealed ampoule at room temperature. After removal of the ethylene oxide and water, the oily residue was fractionally distilled. We obtained 18.3 g (85.1 %) of a slightly yellowish, immobile oil with b.p. 153-156° (0.5 mm), $n_D^{19.5}$ 1.4989 , d^{24} 0.9951 .

Found % : C 71.79; H 11.73; N 5.48; $H_{act.}$ 0.722. $C_{17}H_{33}O_2N$. Calculated % : C 72.04, H 11.73, N 4.94; $H_{act.}$ 0.705 .

Hydrochloride of 2-[di-(β-chloroethyl)-amino]-4-(2,6,6-trimethylcyclohexenyl)-butane (IV). Into a four-necked flask with a stirrer, a reflux condenser, a thermometer, and a dropping funnel was placed 3 g of N,N-di-β-hydroxyethyldihydro-β-ionylamine (III) in 4 ml of chloroform; the solution was cooled to -10° with a mixture of ice and salt and then a solution of 2.64 g of thionyl chloride in 3 ml of chloroform was added to it dropwise over a period of 12 minutes. At the beginning of the addition, the reaction mixture heated up slightly and the solution became yellow. After addition of the thionyl chloride, the reaction mixture was kept at room temperature for 30 minutes and then heated for 2 hours on a boiling water bath; the solution then became brown. Removal of the chloroform and thionyl chloride in vacuum on a water bath yielded 3.7 g of a crystalline product. Recrystallization from 12 ml of benzene gave 2.5 g (66.1%) of the hydrochloride of N,N-di-(2-chloroethyl)-dihydro- β-ionylamine as fine, colorless crystals with m.p. 142-145°. After further recrystallization from a mixture of benzene and ligroin, the substance had m.p. 150-153°.

Found % : C 57.27; H 9.11; N 3.99; Cl 29.81 . $C_{17}H_{32}NCl_3$. Calculated % : C 57.22; H 9.04; N 3.93; Cl 29.81.

SUMMARY

The hydrochloride of 2-[di-(β-chloroethyl)-amino]-4-(2,6,6-trimethylcyclohexenyl)-butane was synthesized from β-ionone through dihydro-β-ionylamine and 2-[di-(β-hydroxyethyl)-amino]-4-(2,6,6-trimethylcyclohexenyl)-butane.

LITERATURE CITED

[1] V. I. Trusheikina, Voprosy Onkologii 2, 222 (1956).

[2] L. F. Larionov and G. N. Platonova, Voprosy Onkologii 5, 36 (1955).

[3] E. Boyland, Biochem. J. 34, 1196 (1940).

[4] T. Kralt, H. D. Moed, and J. van Dijk, Rec. trav. chim. 77, 177 (1958).

[5] L. Haskelberg, J. Am. Chem. Soc. 70, 2811 (1948).

[6] J. Kandel, Ann. Chim. 11, 73 (1939).

[7] L. Knorr and W. Schmidt, Ber. 31, 1072 (1898).

[8] E. Hanby and H. Rydon, J. Chem. Soc. 513 (1947).

SYNTHESIS OF BENZPYRROLIZIDINES

A. N. Kost, L. G. Yudin, Yu. A. Berlin and A. P. Terent'ev

Moscow State University

The high physiological activity of pyrrolizidines has prompted a large number of investigations of the synthesis of substances from this group. However, condensed systems of the benzpyrrolizidine type (I) have hardly been studied.
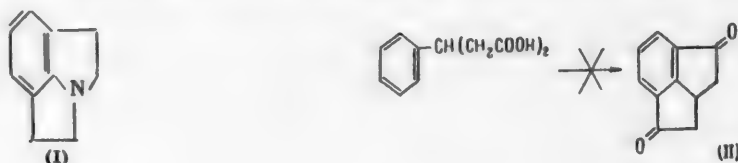
Their formation apparently involves the production of considerable strain as was confirmed by Jackson and Kenner's [1] unsuccessful attempt to synthesize the carbocyclic benzpyrrolizidine analog (II).

The same authors attempted double cyclization of anthranyldiacetic acid but were unable to isolate the desired diketobenzpyrrolizidine (III).
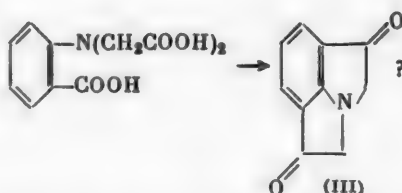
Preston and Tucker [2] synthesized the hydrazone of N-aminocarbazole and cyclohexanone, and treatment of this with hydrochloric acid formed the pentacyclic compound (IV); however, the structure of the latter was not proved.
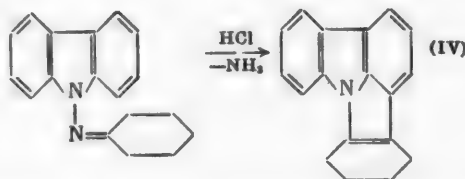
In previous work [3] we showed that the hydrazone of 1-aminotetrahydroquinoline readily underwent the Fischer reaction to form tri- and tetracyclic lilolidine structures.

We chose the following route for the preparation of benzpyrrolizidine derivatives. Reduction of substituted indoles with zinc in hydrochloric acid yielded 2-methyl- and 2-phenylindolines in yields of 70 and 60%, respectively (these syntheses have been described [4, 5] but the yields of the compounds obtained were not given). The action

of sodium nitrite on acid solutions of the indolines gave nitrosamines in yields close to quantitative. The reaction was carried out at 0° to prevent oxidation of the indoline to indole and also migration of the nitroso group to position 5. The latter process occurs particularly readily under the action of hydrogen chloride [6] and therefore sulfuric acid was used as solvent.

Wenzing [4] described the preparation of 1-amino-2-methylindoline by reduction of the nitrosamine with zinc and acetic acid in methanol at 10−15° (yield not given). On attempting to repeat this synthesis, we showed that the yield of the amino derivative did not exceed 10−15% and the bulk of the reaction product was 2-methyl-indoline. The reaction conditions were evidently too drastic and led to rupture of the hydrazine bond. By reducing the temperature to -10°, we obtained 1-amino-2-methylindoline in 80% yield. 1-Aminoindoline (60%) and 1-amino-2-phenylindoline (70%) were obtained analogously.

R = H, CH₃, C₆H₅.
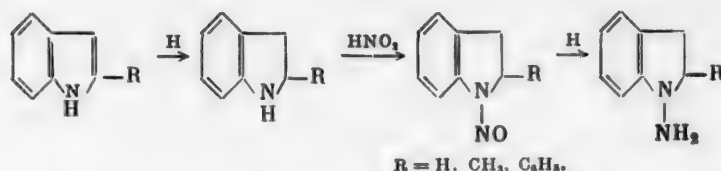
The 1-aminoindolines, which were normal arylalkylhydrazines, reacted with carbonyl compounds to form hydrazones, which underwent the Fischer rearrangement with the elimination of ammonia under the action of acid reagents (for example, sulfuric acid).

(V) R = H, R₁ = CH₃, R₂ = n-C₃H₇.
(VI) R = H, R₁ = CH₃, R₂ = C₆H₅.
(VII) R = R₁ = R₂ = CH₃.
(VIII) R = R₂ = CH₃, R₁ = C₂H₅.
(IX) R = R₁ = CH₃, R₂ = C₆H₅.
(X) R₁ = R₂ = CH₃, R = C₆H₅.
(XI) R = C₆H₅, R₁ = CH₃, R₂ = n-C₃H₇.

(XII) R = H, (XIII) R = CH₃, (XIV) R = C₆H₅.
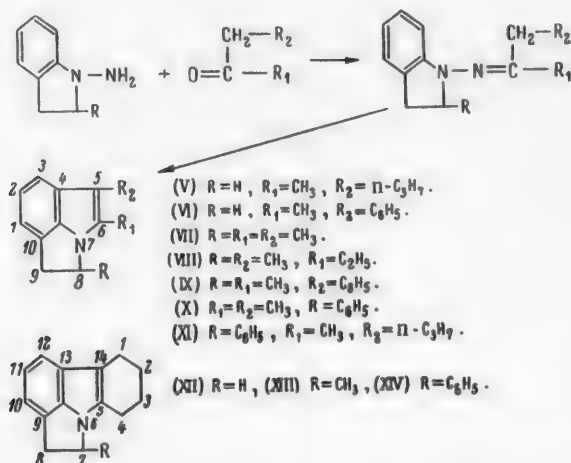
In analogy with benzpyrrocolines and benzquinolizines, we called the compounds of the indole series obtained (V−XI), benzpyrrolizines; analogous compounds (XII−XIV), synthesized from appropriate aminoindolines and cyclo-hexanone, were called pyrrocarbazoles. We numbered the atoms in accordance with systematic rules [7].

Thus, a series of tri- and tetracyclic compounds of previously unknown type were synthesized. There is actually in the literature a report [8] of a synthesis of this type and the authors stated that by reduction of a mix-ture of N-nitrosoindoline and cyclohexanone with zinc in acetic acid they were able to obtain compound (XII) and reported m.p. 154° for it. However, this compound which we obtained from 1-aminoindoline has m.p. 169.5−170°. If we assume that the authors of the work cited carried out a Fischer condensation without isolating the N-aminoindoline, then there are grounds for considering that they were dealing with another reaction product or a complex mixture.

The structure of the compounds we synthesized was confirmed by study of the ultraviolet spectra. Comparison of their absorption spectra with those of 1,2-dimethylindole and lilolidines [3], which have a characteristic absorp-tion maximum in the region of 290 mµ, indicated that the benzpyrrolizidines have a similar structure.

The hydrazones we obtained were converted into indoles quite smoothly if readily enolizable aliphatic and alicyclic ketones were used as the carbonyl compound. In these cases the indole yield reached 76% after the

hydrazone had been boiled with dilute sulfuric acid for even half an hour. A different picture was observed for hydrazones of aliphatic-aromatic ketones and aldehydes. The hydrazones obtained by reaction of 1-amino-2-methylindoline with acetophenone and propiophenone, and also with propionaldehyde, butyraldehyde, isovaleraldehyde, and phenylacetaldehyde were not converted into benzpyrrolizines when boiled with dilute sulfuric acid. The extreme stability of the hydrazones of the aldehydes is interesting, for they were recovered completely (with the exception of the hydrazone of phenylacetaldehyde, of which only half was recovered). An attempt to prepare benzpyrrolizidines from the hydrazones of aldehydes under more drastic conditions (zinc chloride as catalyst at 180— 200°) was also unsuccessful. Distillation of the reaction products gave 2-methylindole, 2-methylindoline, the corresponding hydrazone, and also a small amount of a high-boiling fraction which we were unable to identify. As condensing agents we also used an alcohol solution of hydrogen chloride, boron trifluoride, polyphosphoric acid, etc. The results showing the relative ease of cyclization of different hydrazones agree with modern opinions on the structure and reactivity of hydrazones [9], according to which aryl- and arylalkylhydrazones of aliphatic and alicyclic ketones exist in an enehydrazine form, while hydrazones of aldehydes and aliphatic-aromatic ketones exist in the true hydrazone form with the activation energy of the bonds of the latter considerably higher than in the case of the enehydrazine form.

EXPERIMENTAL *

1-Nitrosoindoline. 18.5 g of indoline (b.p. 100—101° at 12 mm, obtained by catalytic hydrogenation of indole) was dissolved in 125 ml of sulfuric acid (1 : 4) and an aqueous solution of 11.2 g of sodium nitrite added at from -2 to 0° with stirring. The nitrosamine precipitate was carefully washed with water on a filter until the filtrate gave a negative reaction for nitrite ion. We isolated 22.6 g of 1-nitrosoindoline as a light-yellow, finely crystalline powder with m.p. 83°. The yield was quantitative. Literature data [10]: m.p. 83—84°.

1-Nitroso-2-methylindoline was obtained analogously in quantitative yield. The m.p. was 54—55°. Literature data [6]: m.p. 54—55°.

1-Nitroso-2-phenylindoline. This compound was obtained analogously as a thick oil which crystallized when washed with a small amount of alcohol. The m.p. was 99.5— 100.5° (from ligroin with b.p. 60—90°); the yield was 97%.

Found %: N 12.33, 12.44. $C_{14}H_{12}ON_2$. Calculated %: N 12.49.

1-Aminoindoline. A solution of 17.4 g of 1-nitrosoindoline in 200 ml of methyl alcohol was stirred vigorously and kept at from -12 to -7° (external cooling with snow and salt) while 105 ml of acetic acid and 60 g of zinc dust were added in small portions over a period of 4 hours. When half the zinc and acid had been added, the reaction mixture became thick, due to the liberation of zinc acetate; the mixture was diluted with 30 ml of water and stirring continued at room temperature for a further 3 hours. The unreacted zinc was rapidly removed by filtration, the methyl alcohol removed in vacuum, and the residue made strongly alkaline with 40% sodium hydroxide solution while cooled with water, and extracted with ether. The alkali-dried ether extracts were fractionated in vacuum. We isolated 9.4 g (60%) of 1-aminoindoline.

Ultraviolet absorption spectra.

1) 1,2-Dimethylindole, 2) 1,2,3,4,6,7,8,9-octahydropyrido-(1,m-1,2,3)-carbazole, 3) 1,2,3,4,6,7,8-H-pyrro-(1,m-1,2,3)-carbazole, 4) 6-methyl-5-phenyl-7,8,9-H-benz(gh)pyrrolizine.

B.p. 110—112° (12 mm), n_D^{20} 1.5922, d_4^{20} 1.0845, MR_D 41.88; calc. 41.70.

The substance crystallized on prolonged cooling and gave colorless needles with m.p. 5—6°.

The hydrochloride had m.p. 201—203° (decomp.) (from alcohol).

Found %: C 56.55, 56.71; H 6.02, 6.03. $C_8H_{11}N_2Cl$. Calculated %: C 56.30; H 6.50.

---

* For preliminary communication by authors, see [11].

1-Amino-2-methylindoline. A similar reduction of 32.4 g of the nitrosamine gave 22.4 g of 1-amino-2-methylindoline (80% yield). The m.p. was 41°. Literature data [4]: m.p. 41°.

The picrate had m.p. 160—161° (decomp.) (from alcohol).

1-Amino-2-phenylindoline. 18 g of 1-nitroso-2-phenylindoline in 300 ml of methyl alcohol was reduced with 38 g of zinc dust and 70 ml of acetic acid at a temperature of from -12 to -7° over a period of 6.5 hours. The methyl alcohol was removed and the reaction mixture made alkaline and extracted with ether. Removal of the ether gave 10.3 g (64%) of 1-amino-2-phenylindoline. The m.p. was 95.5— 97° (from alcohol). A mixture with 1-nitroso-2-phenylindoline melted at 65°.

Found %: N 12.84, 12.99. $C_{14}H_{14}N_2$. Calculated %: N 13.30.

The hydrochloride had m.p. 193—194° (from alcohol).

1,2,3,4,6,7,8-H-Pyrro-(1,m-1,2,3)-carbazole (XII). A mixture of 1.34 g of 1-aminoindoline and 0.98 g of cyclohexanone was heated for 30 minutes on a boiling-water bath. To the hydrazone obtained was rapidly added 10 ml of 20% sulfuric acid (both substances were first heated to ~100°). A voluminous precipitate formed after a few seconds. The mixture was heated on the boiling water bath for a further 20 minutes and cooled to room temperature and the precipitate collected and carefully washed on a filter with water to remove the 1-aminoindoline sulfate formed. We isolated 1.15 g (60%) of a substance with m.p. 169.5—170° (from alcohol).

Found %: C 85.00, 85.00; H 8.08, 7.85; N 6.90, 7.00. $C_{15}H_{15}N$. Calculated %: C 85.23; H 7.66; N 7.10.

λ_{max} 234, 292 mμ, lg ϵ 4.40, 3.86 (in methanol).

7-Methyl-1,2,3,4,6,7,8H-pyrro(1,m-1,2,3)-carbazole (XIII). By a similar procedure, from 2.9 g of 1-amino-2-methylindoline and 1.9 g of cyclohexanone we obtained 3 g (70%) of (XIII) with m.p. 87—87.5° (from alcohol).

Found %: C 84.83, 84.92; H 8.30, 8.18; N 6.70, 6.90. $C_{15}H_{17}N$. Calculated %: C 85.26; H 8.11; N 6.63.

λ_{max} 232, 291 mμ, lg ϵ 4.50, 3.92 (in methanol).

The picrate had m.p. 137—137.5° (decomp.) (from alcohol).

Found %: C 57.32, 57.52; H 4.82, 4.74. $C_{21}H_{20}O_7N_4$. Calculated %: C 57.27; H 4.58.

7-Phenyl-1,2,3,4,6,7,8H-pyrro(1,m-1,2,3)carbazole (XIV). The interaction of 1.0 g of 1-amino-2-phenyl-indoline and 0.47 g of cyclohexanone yielded 1 g (76%) of (XIV) with m.p. 109.5—110° (from alcohol).

Found %: C 87.93, 88.01; H 7.03, 7.06; N 5.18, 5.19. $C_{20}H_{19}N$. Calculated %: C 87.87; H 7.01; N 5.13.

λ_{max} 230, 292 mμ, lg ϵ 4.51, 3.89 (in methanol).

6-Methyl-5-n-propyl-7,8,9H-benz(gh)pyrrolizine (V). The hydrazone obtained by heating a mixture of 1.025 g of 1-aminoindoline and 0.75 g of methyl butyl ketone on a boiling-water bath for 3 hours, and then removing the excess ketone in vacuum, was treated in the usual way (heating with 10 ml of 20% sulfuric acid for 40 minutes) to yield 0.60 g (40%) of a substance with m.p. 96—97° (from alcohol).

Found %: C 84.34, 84.43; H 8.74, 8.75; N 6.99, 7.14. $C_{14}H_{17}N$. Calculated %: C 84.37; H 8.60; N 7.03.

λ_{max} 234, 294 mμ, lg ϵ 4.55, 3.84 (in methanol).

6-Methyl-5-phenyl-7,8,9H-benz(g,h)pyrrolizine (VI). The usual treatment of the hydrazone obtained by heating a mixture of 0.67 g of 1-aminoindoline and 0.67 g of phenylacetone yielded 0.75 g (65%) of a benzpyrrol-izine with m.p. 145—146° (from alcohol).

Found %: C 87.41, 87.52; H 6.40, 6.50; N 6.07, 6.27. $C_{17}H_{15}N$. Calculated %: C 87.51; H 6.48; N 6.00.

λ_{max} 232, 293 mμ, log ϵ 4.64, 4.31 (in methanol).

5,6,8-Trimethyl-7,8,9H-benz(g,h)pyrrolizine (VII). Similarly, from 2.96 g of 1-amino-2-methylindoline and 1.44 g of methyl ethyl ketone we obtained 1.6 g (43%) of (VII) with m.p. 51—51.5° (from alcohol).

Found %: C 83.67, 83.79; H 8.11, 8.17; N 7.63, 7.72. $C_{13}H_{15}N$. Calculated %: C 84.26; H 8.16; N 7.56. λ_{max} 231, 292 mμ, lg ϵ 4.42, 3.87 (in methanol).

5,8-Dimethyl-6-ethyl-7,8-9H-benz(g,h)pyrrolizine (VIII). From 2.96 g of 1-amino-2-methylindoline and 1.72 g of diethyl ketone we obtained 1.3 g (32%) of (VIII) with m.p. 28.5—29° (from alcohol).

Found %: C 83.93, 83.95; H 8.67, 8.71; N 7.20, 7.42. $C_{14}H_{17}N$. Calculated %: C 84.38; H 8.60; N 7.03. λ_{max} 232, 292 mμ, lg ϵ 4.44, 3.89 (in methanol).

6,8-Dimethyl-5-phenyl-7,8,9H-benz(gh)pyrrolizine (IX). Reaction of 1.42 g of 1-amino-2-methylindoline and 1.34 g of phenylacetone in the usual way gave 1.3 g (53%) of (IX) with m.p. 79—80° (from alcohol).

Found %: C 87.05, 87.25; H 6.92, 7.03; N 5.46, 5.51. $C_{19}H_{17}N$. Calculated %: C 87.41; H 6.93; N 5.66. λ_{max} 235, 275 mμ, lg ϵ 4.52, 4.24 (in methanol).

5,6-Dimethyl-8-phenyl-7,8,9H-benz(gh)pyrrolizine (X). Similarly, 0.7 g of 1-amino-2-phenylindoline and 0.5 g of methyl ethyl ketone yielded 0.55 g (69%) of (X) with m.p. 116—117° (from alcohol).

Found %: C 87.17, 87.32; H 7.09, 7.01. $C_{19}H_{17}N$. Calculated %: C 87.41; H 6.93.

λ_{max} 230, 295 mμ, lg ϵ 4.46, 3.94 (in methanol).

6-Methyl-5-n-propyl-8-phenyl-7,8,9H-benz(gh)pyrrolizine (XI). By the usual method, from 0.7 g of 1-amino-2-phenylindoline and 0.33 g of methyl butyl ketone we obtained 0.6 g (66%) of (XI) with m.p. 87° (from alcohol).

Found %: N 5.07, 5.08. $C_{20}H_{21}N$. Calculated %: N 5.09.

λ_{max} 230, 293 mμ, lg ϵ 4.57, 3.91 (in methanol).

SUMMARY

1. Procedures were developed for preparing substituted N-aminoindolines in yields of 60—80%.

2. A method was proposed for synthesizing tri- and tetracyclic compounds of the benzpyrrolizine series.

LITERATURE CITED

[1] J. Jackson and J. Kenner, J. Chem. Soc. 1928, 573.

[2] R. Preston and S. Tucker, J. Chem. Soc. 1943, 659.

[3] A. N. Kost, L. G. Yudin, and A. P. Terent'ev, Zhur. Obshchei Khim. 29, 1949 (1959).*

[4] M. Wenzing, Lieb. Ann. 239, 239 (1887).

[5] E. Fischer and T. Schmitt, Ber. 21, 1071 (1888).

[6] O. Jackson, Ber. 14, 879 (1881).

[7] A. P. Terent'ev, A. N. Kost, A. M. Tsukerman, and V. M. Potapov, Systematic Nomenclature of Organic Compounds [in Russian] (Academy of Sciences USSR Press, 1955).

[8] F. Lions and E. Ritchie, J. Am. Chem. Soc. 61, 1927 (1939).

[9] A. E. Arbuzov and Yu. P. Kitaev, Zhur. Obshchei Khim. 27, 2338 (1957).*

[10] G. Plancher and C. Ravenna, Atti Linc. (5), 14, I, 636 (1905); Zbl. II, 335 (1905).

[11] L. G. Yudin, A. N. Kost and Yu. A. Berlin, Khim. Nauka i Prom. 3, 406 (1958).

* Original Russian pagination. See C. B. translation.

INVESTIGATION OF THE MECHANISM OF HYDROCARBON OXIDATION
BY CHROMYL CHLORIDE

L. V. Sulima and I. P. Gragerov

Institute of Physical Chemistry, Academy of Sciences Ukrainian SSR

It is possible to obtain substituted benzaldehydes from toluene and its derivatives, quinones from aromatic hydrocarbons, and glycol chlorohydrins from olefins by oxidation with chromyl chloride. In addition to these conversions, which have preparative value, reactions with paraffins, glycols, and terpenes, which are more complex and give oxidation, chlorination, and isomerization products, are interesting [1]. The reaction examined, which was first studied by Etard [2], normally proceeds in two stages: chromyl chloride forms a complex with the substrate and in most cases this has a definite composition and forms a precipitate, which reacts with water to form oxidation products and a mixture of chromium compounds. The oxidation is almost always accompanied by chlorination and in some cases the complex gives the starting organic substances when treated with water.

The mechanism of the Etard reaction, which is of particular interest due to its connection with the mechanism of oxidation by other chromium compounds, has not been elucidated. In particular, the structure of the Etard complexes and how they react with water are not known. In order to solve these problems, in the present work complexes of chromyl chloride with cyclohexene, benzene, triphenylmethane, and toluene were decomposed with heavy-oxygen-labeled water. It was found that the chlorocyclohexanol and quinone produced contained oxygen only from the oxidant but $70-80\%$ of the oxygen in the triphenylcarbinol came from the water and $20-30\%$ of the oxygen from the oxidant. The latter result was confirmed by hydrolysis of the triphenylmethane complex with $CrO_2^{18}Cl_2$ by ordinary water. The same $70-80\%$ of oxygen from the water was found when the triphenylmethane complex, which had lost part of the chlorine as a result of preliminary heating, was hydrolyzed with heavy-oxygen-labeled water, H_2O^{18}. The route by which oxygen is transferred in the oxidation of toluene could not be determined, due to the rapid exchange of oxygen of water with the benzaldehyde formed. This exchange was confirmed by special experiments.

In addition to experiments with H_2O^{18}, a study was made of the decomposition by heavy-hydrogen-labeled water, D_2O, of the compound of chromyl chloride with o-nitrotoluene, which is an example of a complex regenerating the starting organic compound. In this experiment it was found that deuterium was not incorporated into the o-nitrotoluene formed. Finally, it was shown that complexes of chromyl chloride with triphenylmethane and o-nitrotoulene also regenerate the original organic substances when treated with ether.

$$
\begin{array}{ll}
\ce{H2C-CH2-CH-Cl} & \ce{HO}\diagdown \\
\text{structure} & \ce{Cl-Cr-O-\text{[ring]}-O-Cr-Cl} \; ; \\
\end{array}
$$

$$
C_6H_5CH \left(-O-Cr{<}{OH \atop Cl} \; Cl \right)_2 \; ; \qquad (C_6H_5)_3C-O-Cr{<}{OH \atop Cl} \; Cl \; .
\tag{1}
$$
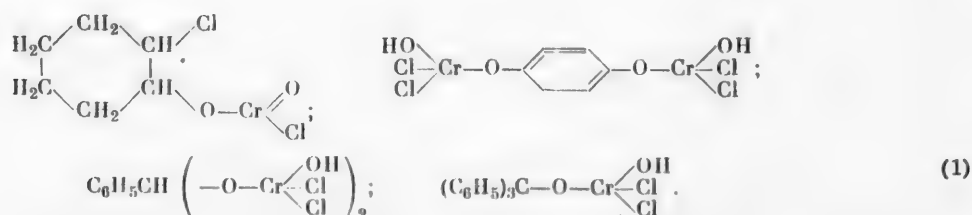
Our results agree with the ester-type structure of Etard complexes proposed by Etard himself only on the basis of analysis results and by Cristol and Eilar [3] for compounds with olefins*.

If such a structure is assumed, then the action of water consists of hydrolysis of the ester-like compounds. The direction of this reaction may be predicted on the basis of the data of Dostrovsky et al. [5], which showed that in the hydrolysis of esters of inorganic acids, the alkyl—oxygen bond was never broken if the element X was in the maximum valence state.

$$R{\mid}O{-}X + H{\mid}O^{18}H \rightarrow R{-}O^{18}H + X{-}OH$$
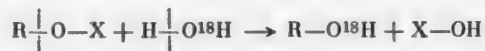
Since chromium is tetravalent in compounds of type (1), it is to be expected that these compounds will be hydrolyzed by the other route, namely, with breakage of the acyl—oxygen bond, and that the oxygen from the oxidant and not from the water will be incorporated into the oxidized organic product.

$$R{-}O{\mid}X + H{\mid}O^{18}H \rightarrow R{-}OH + X{-}O^{18}H \tag{2}$$
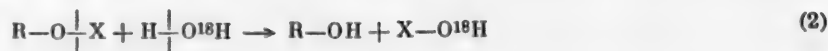
We obtained precisely this result on decomposing complexes of benzene** and cyclohexene by the action of H_2O^{18} and we consider that it confirms the structure of complexes of type (1). The different result in experiments with triphenylmethane we explain (see above) by the fact that in this case, and similarly for many o-substituted toluenes, the oxidation in the Etard reaction is accompanied by considerable chlorination (which sometimes involves steric hindrance [1])and the H_2O^{18} hydrolyzes both the triphenylmethyl chloride produced, giving carbinol containing O^{18}, and also a compound of type (1), giving normal carbinol.

The formation of chloro derivatives in the Etard reaction is apparently connected with the fact that in addition to hydrolysis, the action of water on complexes with chromyl chloride always produces (to a greater or lesser extent) homolytic decomposition. This hypothesis is supported by the oxidation of glycols by chromyl chloride [6] and certain oxidation reactions of chromic acid [7] and also by the regeneration of triphenylmethane and o-nitrotoluene we observed when their chromyl chloride complexes were treated with dry ether, which is difficult to explain by any nonradical process.

As regards the Etard complexes which regenerate the starting organic substances when treated with water, our experiments with D_2O showed that this complex of o-nitrotoluene cannot have structure (1) as the o-nitrotoluene formed from it did not contain deuterium. For the same reason, the complex cannot have structure (3), proposed by Slack and Waters [8]***.

$$o{-}O_2N{-}C_6H_4CH\left(-Cr\begin{matrix}OH\\O\\Cl\\Cl\end{matrix}\right)_2 \tag{3}$$

---

* The latter authors conclusively disproved the formulas of Sword [4] of the form:

$$R{-}CH{-\!-\!-\!-}CH{-}R' \qquad R{-}CH{-}CH{-}R'$$

and

$$Cl_2Cr{-}O{-}O{-}CrCl_2 \qquad Cl_2\,Cr{-}O \quad O{-}Cr\,Cl_2$$
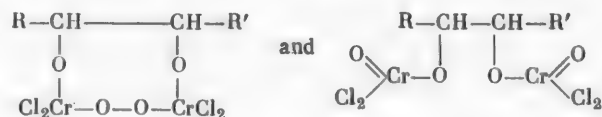
** The hydroquinone formed from the benzene was converted into quinone by the elimination of hydrogen and the quinone was analyzed for O^{18} content.

*** Slack and Waters considered that compounds of this type, which are stable for o-nitrotoluene, are also formed in other cases of the Etard reaction and in oxidation with CrO_3, but are usually unstable and rearrange rapidly into substances of type (1). Formulas of type (3) were previously proposed [8] for Etard complexes and rejected on the grounds that the complexes differ sharply from organochromium compounds.

Thus, the problem of the structure of complexes of the type considered remains unsolved and it can only be assumed that they have a structure differing from that of normal Etard complexes.

We should note that Hartford and Darrin [1] recently proposed that chromyl chloride in complexes is bound to the organic molecule by hydrogen bonds, for example:

$$C_6H_5CH \begin{matrix} H \cdots\cdots O=Cr\begin{matrix} O \\ Cl_2 \end{matrix} \\ | \\ H \cdots\cdots O=Cr\begin{matrix} O \\ Cl_2, \end{matrix} \end{matrix}$$
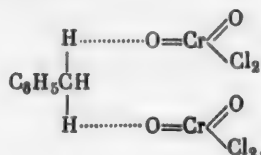
and attempted to explain all the facts on the Etard reaction from this point of view. These hypotheses explain why deuterium is not incorporated in the regenerated o-nitrotoluene when the complex of o-nitrotoluene with CrO_2Cl_2 is decomposed by D_2O. However, in our opinion they are unacceptable, as the energy of a hydrogen bond of the type $CH \cdots O$ is very small even in the most favorable cases, and the formation of Etard complexes is accompanied by considerable heat evolution. In addition, hydrogen bonds are known to be more stable the greater the tendency of the hydrogen to ionize, and it would be expected that complexes with nitrotoluenes, and especially with dinitro-toluenes and chloroform would form particularly readily, which does not correspond to experiment either. The aspects examined only formally describe the reaction and essentially give no information on its mechanism.

EXPERIMENTAL

Reagents. The chromyl chloride was prepared by the action of a mixture of hydrochloric and sulfuric acids on chromic anhydride [9] and after distillation it had b.p. 115—116°. (750 mm). $CrO_2^{18}Cl_2$ was obtained by the same method but with H_2O^{18} used as a solvent for the CrO_3 and hydrogen chloride. Benzene, toluene, cyclohexene, o-nitrotoluene, ether, carbon tetrachloride, ligroin, and chloroform were carefully dried and distilled. Triphenyl-methane was recrystallized from CCl_4 and had m.p. 92°. Heavy-oxygen-labeled water contained about 1.2 at. % excess O^{18} and the heavy-hydrogen labeled water, 20% of D.

Oxidation of toluene. The complex of toluene and chromyl chloride was prepared according to Etard's method by the slow addition of a 10% solution of 0.4 mole of CrO_2Cl_2 in chloroform to a heated 10% solution of 0.2 mole of toluene in the same solvent. The precipitate was washed with CCl_4, the remainder of which was removed in vacuum. The complex was hydrolyzed by different methods. In the first series of experiments it was hydrolyzed by water at 20° and at 0°, or by 3% CH_3COONa at 0°; in the second series it was hydrolyzed by concentrated solutions of NaCl or $CaCl_2$, cooled to partial freezing. In the first series of experiments 7 g of complex was introduced in small portions into 10 g of H_2O^{18} and the benzaldehyde was extracted with ether and then distilled after removal of the solvent. It had b.p. 70—72° (30 mm), n_D^{20} 1.545—1.549; the yield was 1 g. In the second series of experiments, to a mixture of 2—3 g of complex and 10 ml of CCl_4 (or 9 ml of $CCl_4 +$ 1.5 ml of ligroin in experiments with $CaCl_2$) in a separating funnel frozen with liquid air was added a partially frozen solution of 8.25 g of NaCl in 25 ml of H_2O^{18} (at a temperature of -21°) or 22 g of $CaCl_2 \cdot 6H_2O$ in 16 ml of H_2O^{18} (at about -40°). The reaction occurred with shaking for a few minutes at a temperature between -20 and -10° in experiments with NaCl and at a temperature between -40 and -20° with $CaCl_2$. The organic layer was then separated at 0°, the solvent rapidly removed in vacuum at the same temperature, and the aldehyde distilled. It had n_D^{20} 1.547—1.548; the yield was 0.3—0.5 g.

The benzaldehyde from experiments of both series contained 0.6—0.9% excess O^{18}. Since this result could have depended on isotope exchange of the aldehyde with H_2O^{18}, we studied this exchange at temperatures and acidities close to those of our experiments: a mixture of 0.8 g of benzaldehyde and 10 ml of CCl_4 was frozen in a separating funnel; to it was added a partially frozen solution of 8.25 g of NaCl in 25 ml of 0.3 N HCl, prepared from H_2O^{18}; after being shaken for 3 minutes at a temperature between -20 and -10°, the aldehyde was isolated as described above for experiments with NaCl solutions. This aldehyde contained 0.6% excess O^{18}. Thus, isotopic exchange was so considerable that it was impossible to determine the source of the oxygen in the oxidation of toluene to benzaldehyde.

Oxidation of cyclohexene. A mixture of 32.0 g of chromyl chloride in 32 ml of CCl_4 was added dropwise with stirring to a solution of 16.2 g of cylcohexene in 40 ml of CCl_4 at 0—5° [3]. The precipitate of complex

was washed with CCl_4 and the solvent removed from the precipitate in vacuum. 30 g of complex was introduced in small portions into a solution of 10 g of sodium pyrosulfite in 80 ml of H_2O^{18}, cooled to 0°. After separation of the organic layer, the aqueous layer was extracted twice with ether, the combined extracts dried with Na_2SO_4, the solvent removed, and the residue distilled. The fraction distilling at 90—105° (24 mm) was redistilled to give chlorocyclohexanol with b.p. 92—95° (24 mm), n_D^{20} 1.4906; d_4^{25} 1.3355. This substance did not contain excess O^{18}. Consequently, its oxygen was derived from the oxidant.

Oxidation of benzene. To 25 ml of benzene was added 5.9 g of chromyl chloride in five portions over a period of 3 hours in the cold. After a day the precipitate of complex was collected and washed with benzene, the excess of which was removed in vacuum [2]. The yield was 2.3 g. A suspension of 0.8 g of complex in 5 ml of chloroform was frozen in a separating funnel, and to it was added a partially-frozen solution of 3.3 g of NaCl in 10 ml of H_2O^{18}. The contents of the funnel were shaken and the reaction was complete in 3 minutes while the temperature rose from -21 to -2°. The chloroform layer was separated, the solvent removed in vacuum, and the quinone sublimed. Its m.p. was 115—116°; the yield was about 0.1 g. The quinone contained 0.15% excess O^{18}. A control experiment showed that when a chloroform solution of quinone was shaken with H_2O^{18} at a similar temperature and acidity, the quinone acquired about 0.1% excess O^{18}. Hence it follows that the excess O^{18} in the quinone obtained by oxidation of benzene was caused by isotopic exchange with the water and that the oxygen in the quinone was derived from the oxidant and not the water.

Oxidation of triphenylmethane. A 20% solution of CrO_2Cl_2 in CCl_4, in an amount corresponding to 1.5 mole of oxidant to 1 mole of hydrocarbon, was added slowly with stirring to a 10% solution of triphenylmethane in CCl_4 at a temperature of not more than 20°. The complex was collected after 12 hours, washed with CCl_4, and the residual solvent removed in vacuum [10]. The complex was decomposed by introducing it in small portions, with stirring, into a dilute solution of NaOH in H_2O^{18} *. The precipitate of triphenylcarbinol and chromium hydroxide was dried in a vacuum over P_2O_5 and the carbinol extracted with boiling CCl_4 and purified by recrystallization from the same solvent. Its m.p. was 162° and the yield about 90%. The table gives the conditions and results of typical experiments.

Decomposition of Etard Complexes of Triphenylmethane with H_2O^{18}

Amount of substance (in g)			Excess O^{18} content (in %)		Amount of oxygen passing into the carbinol from the water (in %)
complex	H_2O^{18}	NaOH	in alkali solution	$(C_6H_5)_3OH$ obtained	
6.5	30	3.0	1.07	0.85	79
6.1	30	3.0	1.09	0.88	81
7.0	30	3.0	1.05	0.86	82
7.4	30	3.0	1.12	0.81	72
7.3	30	3.0	1.23	0.96	79
7.0	30	3.0	1.03	0.75	73
15.0	50	7.0	1.09	0.87	80
2.9 *	30	—	—	0.08	88

* In this experiment the CrO_2Cl_2 incorporated in the complex contained 0.7% excess O^{18} and normal water was used for the hydrolysis.

In a separate experiment, 8 g of complex was heated for 1 hour at 80°. The substance, which lost part of its chlorine as HCl, was decomposed with H_2O^{18} as described above. In this case about 80% of the oxygen in the triphenylcarbinol formed was derived from the water.

Then 11.2 g of complex was decomposed not with water but with absolute ether (50 ml). The ether was then removed in vacuum and the dry residue extracted with benzene. After removal of the benzene in vacuum, the residue was recrystallized from a mixture of benzene and ligroin (1 : 1) and then twice from CCl_4. This gave 0.1

* The alkali was necessary to suppress isotopic exchange of the triphenylcarbinol with water [5]. We established that this exchange occurs even at room temperature in acid solutions.

g of triphenylcarbinol with m.p. 159—160°. Evaporation of the combined mother liquors yielded 6 g of impure triphenylmethane with m.p. 85°, which was recrystallized from CCl_4 to give pure substance with m.p. 92°, undepressed by admixture with pure triphenylmethane.

Interaction of chromyl chloride with o-nitrotoluene. A mixture of 9.6 g of chromyl chloride and 1 ml of CCl_4 was added over a period of 3 minutes to a solution of 10 g of o-nitrotoluene in 50 ml of CCl_4 at room temperature. After several days the precipitated complex was collected, washed with CCl_4, and the residual solvent removed in vacuum [10]. 11.8 g of complex was introduced in small portions, with cooling, into 30 ml of 20% D_2O. The reaction mixture was extracted with CCl_4, the extracts dried with $CaCl_2$, and the solvent removed. Distillation of the residue yielded about 2 g of o-nitrotoluene with b.p. 71—72° (5 mm) and n_D^{20} 1.5463. The reaction products also contained small amounts of o-nitrobenzaldehyde and chloro derivatives. Isotopic analysis showed that the o-nitrotoluene isolated did not contain excess deuterium.

In another experiment, decomposition of 14 g of complex with 50 ml of absolute ether also regenerated about 2 g of o-nitrotoluene.

Isotopic analysis. The chlorocyclohexanol was analyzed for O^{18} content by a method developed by one of us [11], consisting of cracking and heating a sample of the substance in a quartz ampoule in an atomospher of a given amount of CO_2 of normal isotopic composition and then determining mass spectrometrically the O^{18} content of the CO_2, which had acquired an equilibrium amount of this isotope. However, as a special test showed, this method was unsuitable for accurate analysis of benzaldehyde, quinone, and triphenylcarbinol. Therefore, without distortion of their isotopic composition, these substances were converted into a form suitable for analysis; the benzaldehyde was heated in an empty sealed glass ampoule for 6 hours at 350° and the quinone was heated in the same way for 4 hours at 250°. Tests showed that the products produced by heating (mainly benzyl benzoate, and hydroquinone) could be analyzed satisfactorily by the above method. For analysis of triphenylcarbinol, a slow stream of hydrogen chloride, carefully dried over P_2O_5, was passed through a boiling benzene solution of the carbinol. The water formed* was distilled, made alkaline with metallic sodium in a dry nitrogen atmosphere, again distilled from the salt and alkali, and analyzed in a mass spectrometer [12]. Control experiments confirmed that this method gave satisfactory results.

For determination of deuterium in o-nitrotoluene, the latter was burned over copper oxide and the excess density of the water obtained determined by the flotation method.

SUMMARY

1. When chromyl chloride complexes of cyclohexene, benzene, triphenylmethane, and toluene were decomposed with H_2O^{18}, the chlorocyclohexanol and quinone formed contained oxygen derived only from the oxidant, while about 20% of the oxygen in the triphenylcarbinol was derived from the oxidant and about 80% from the water. The source of the benzaldehyde oxygen could not be determined due to rapid isotopic exchange with water.

2. When the chromyl chloride complex of o-nitrotoluene was decomposed with D_2O, deuterium was not incorporated into the o-nitrotoluene regenerated. When this complex and also the chromyl chloride complex of triphenylmethane were treated with dry ether, o-nitrotoluene and triphenylmethane were regenerated.

3. The data presented agree with an ester-type structure for Etard complexes. The action of water consists of hydrolyzing them at the acyl—oxygen bond, leading to oxidation products. In the case of triphenylmethane, in addition to this reaction, $(C_6H_5)_3CCl$ is apparently formed, and this gives $(C_6H_5)_3CO^{18}H$ on hydrolysis. The formation of the chloro derivative, and also regeneration of triphenylmethane and o-nitrotoluene by the action of dry ether on their complexes is explained by homolytic decomposition of the complex. The structure of the o-nitrotoluene complex remains unelucidated.

LITERATURE CITED

[1] W. H. Hartford and M. Darrin, Chem. Revs. 58, 1 (1958).

[2] A. Etard, Ann. Chim. Phys. (5), 22, 218 (188); C. r. 97, 907 (1883); 116, 434 (1893); 120, 1058 (1895).

[3] S. J. Cristol and K. R. Eilar, J. Am. Chem. Soc. 72, 4253 (1950).

[4] J. Sword, Chem. News 133, 1 (1926).

*Water was formed by the reaction: $(C_6H_5)_3COH + HCl \rightarrow (C_6H_5)_3CCl + H_2O$.

[5] M. Anbar, J. Dostrovsky, D. Samuel, and A. D. Jaffe, J. Chem. Soc. 1954, 3603.

[6] R. Slack and W. A. Waters, J. Chem. Soc. 1949, 594.

[7] R. Slack and W. A. Waters, J. Chem. Soc. 1949, 599.

[8] G. Rohde, Sammelung Chemische und Chemisch-Technischer Vorträge, VI, 241—302, (Stuttgart, 1901) (Cited from [1]).

[9] Inorganic Syntheses [in Russian], 1951, Vol. II, p. 199.

[10] H. D. Law and F. M. Perkin, J. Chem. Soc. 93, 1633 (1908).

[11] I. P. Gragerov, in Collection: Problems in Kinetics and Catalysis, IX,"Isotopes in Catalysis"[In Russian], 1957, p. 373.

[12] A. I. Brodskii, S. G. Demidenko, L. L. Strizhak, and V. R. Lechekhleb, Zhur. Analyt. Khim. 10, 256 (1956).

ISOQUINOLINE COMPOUNDS

I. DERIVATIVES OF ISOMERIC SALSOLIN

I. T. Strukov and O. A. Kolganova

Reserpine [1] is a very complex alkaloid. In this connection there is definite interest in searches for simpler synthetic compounds with hypotensive and sedative (soothing) action among isoquinoline derivatives. Although the isoquinoline series has been studied quite well and many compounds found with application in medicine (papaverine, perperine, salsolin, etc.) it would be advantageous to continue the study of isoquinoline derivatives to obtain new pharmacologically active compounds, tending towards the formation of new preparations from fragments of the reserpine molecule.

In actual fact, the reserpine molecule (I) may be regarded as a condensed system of β-carboline and deca-hydroisoquinoline with an appropriate steric distribution of the groupings. Rupture of the carbon—carbon bond in position 2—3 of reserpine leads to a compound of the decahydroisoquinoline series.

(I)
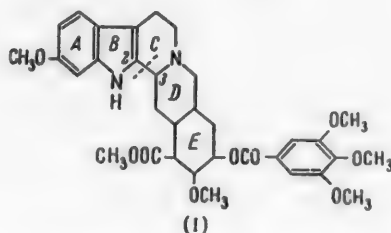
However, there may be considerable difficulties even in the synthesis of such a compound. Work has already been done in this direction, and some compounds have been synthesized, though nothing is known as yet of their pharmacological action [1].

We undertook to prepare first a series of compounds similar in structure to salsolin. For this purpose we prepared 3-methoxy-4-benzyloxyphenylethylamine from vanillin by two methods. One of these consisted of converting vanillin into ferulic acid [2], hydroferulic acid (II), its methyl ester (III), its amide (IV), the amide of 3-methoxy-4-benzyloxyphenylpropionic acid (V), and then (by Helfer's method [3]) into 3-methoxy-4-benzyloxyphenylethyl-amine (VI).
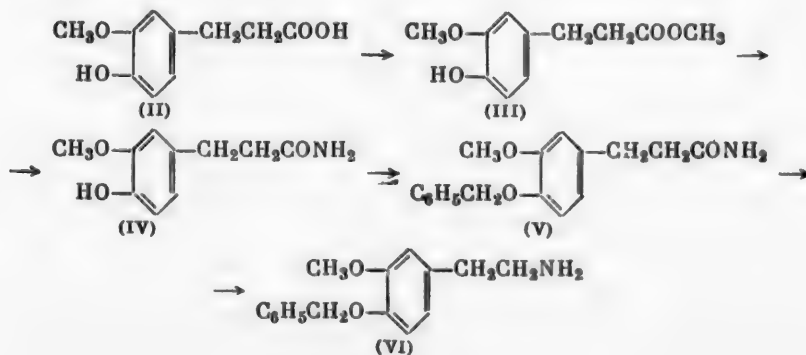
The second and more convenient method of preparing compound (VI) was developed by L. V. Volkova [4], starting from 3-methoxy-4-benzyloxybenzaldehyde, which was converted into 3-methoxy-4-benzyloxybenzyl alcohol (VII) by Davidson and Bogert's method [5], and then into the chloride (VIII), cyanide (IX), and amine (VI).

CH_3O—〇—CHO , $C_6H_5CH_2O$— → CH_3O—〇—CH_2OH , $C_6H_5CH_2O$— (VII) →

→ CH_3O—〇—CH_2Cl , $C_6H_5CH_2O$— (VIII) → CH_3O—〇—CH_2CN , $C_6H_5CH_2O$— (IX) →

→ CH_3O—〇—$CH_2CH_2NH_2$, $C_6H_5CH_2O$— (VI)
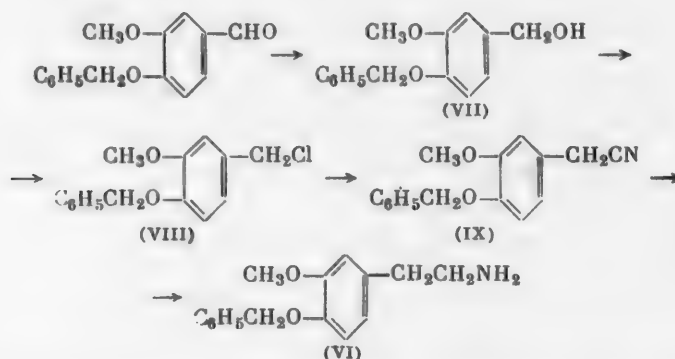
Compound (VI) was used to prepare the acetyl derivative (X) [6], which was converted into 1-methyl-6-methoxy-7-benzyloxy-3,4-dihydroisoquinoline (XI) [7], its iodomethylate (XII), its chloromethylate (XIII), 1,2-dimethyl-6-methoxy-7-hydroxy-1,2,3,4-tetrahydroisoquinoline (XIV), and the 3,4,5-trimethoxybenzoic ester of the latter (XV).

(VI) → (X) → (XI) →

→ (XII) → (XIII) →

→ (XIV) → (XV)
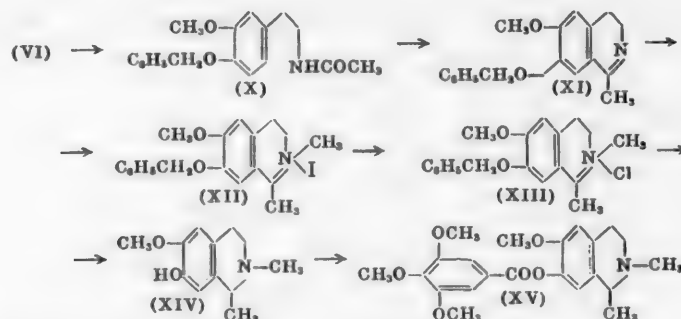
A number of these compounds were sent for pharmacological study.

EXPERIMENTAL

<u>Hydroferulic acid (II)</u>. In contrast to the reduction of ferulic acid with sodium amalgam [8] and with hydrogen in the presence of palladium on calcium carbonate [9], we carried out the hydrogenation in the presence of a nickel catalyst. 63 g of ferulic acid was dissolved in 200 ml of water in the presence of 27 g of sodium carbonate, 10 g of a 60% paste of nickel catalyst added, and hydrogenation carried out at 100° for 4 hours in an autoclave (capacity 1.6 liters) until the hydrogen pressure no longer fell. The catalyst was removed by filtration and the filtrate acidified with concentrated sulfuric acid. The oil liberated rapidly crystallized. The yield of hydroferulic acid was 57.1 g (90.5%). The m.p. was 88—90°.

<u>Methyl ester of hydroferulic acid (III)</u>. A mixture of 53 g of hydroferulic acid, 500 ml of methanol, and 50 ml of concentrated sulfuric acid was heated under reflux for 8 hours. The methanol was removed in vacuum and the residue poured into a separatory funnel containing a mixture of 200 ml of water, 100 g of ice, and 200 ml of ether, and shaken. The ether solution was separated, washed with water and a solution of sodium carbonate, and dried with anhydrous magnesium sulfate. After removal of the ether, the oil was vacuum distilled at 2 mm. The b.p. was 155—157°. The yield was 51 g (90%).

Found %: C 62.60, 62.99; H 6.77, 6.85. $C_{11}H_{14}O_4$. Calculated %: C 62.85; H 6.71.

<u>Amide of hydroferulic acid (IV)</u>. 50 g of the methyl ester of hydroferulic acid was shaken on a mechanical rocker for 2 days with 600 ml of a concentrated aqueous solution of ammonia. Evaporation of the solution to 100

ml yielded 31 g (67%) of the amide of hydroferulic acid. The m.p. was 114—116° (from water).

Found %: N 7.37, 7.20. $C_{10}H_{13}O_3N$. Calculated %: N 7.18.

Amide of 3-methoxy-4-benzyloxyphenylpropionic acid (V). Sodium (4 g) was dissolved in 100 ml of anhydrous alcohol, 31 g of the amide of hydroferulic acid added and after thorough stirring, 22 g of benzyl chloride was introduced. The mixture was heated under reflux on a boiling-water bath for 3 hours. Then 100 ml of alcohol was added and the solution rapidly filtered on a Buchner funnel to remove the precipitate of sodium chloride. On cooling, the filtrate deposited a voluminous precipitate. The following day the precipitate was collected, washed with alcohol, and dried. The yield was 38.6 g (85.2%). The substance formed silky needles (from alcohol). The m.p. was 119—120°.

Found %: N 4.95, 4.91. $C_{17}H_{19}O_3N$. Calculated %: N 4.91.

Compound (V) was previously obtained by heating the ammonium salt of 3-methoxy-4-benzyloxyphenyl-propionic acid at 200—210° [10].

3-Methoxy-4-benzyloxyphenylethylamine (VI). Into a 3-neck, round-bottomed flask of 500 ml capacity with a stirrer were placed 140 ml of water and 44.5 g of potassium hydroxide, the solution cooled to from 0 to +1°, and 16.8 g of bromine gradually added, followed by 30.8 g of the amide of 3-methoxy-4-benzyloxyphenylpropionic acid. After 30 minutes, the temperature of the water bath was raised to 55—60° and kept at this level for 1.5 hours. After cooling, the thick, pasty mass was treated several times with ether (3 × 200 ml). The ether was removed from the extract. The residual oil gradually crystallized. We obtained 9.45 g (34%) of amine (VI) with m.p. 68—70° (from a mixture of ether and ligroin). The hydrochloride formed needles (from alcohol) with m.p. 173—175°.

3-Methoxy-4-benzyloxyphenylethylacetamide (X) was obtained from (VI) by the method of Späth and Orechoff [6]. It formed long, fine, colorless needles (from water, 1 : 200). The m.p. was 116—117°.

1-Methyl-6-methoxy-7-benzyloxy-3,4-dihydroisoquinoline (XI) was obtained from compound (X) by the method of Gullard and Haworth [11]. The yield was 60.5%. The m.p. was 87—88° (from 25% alcohol).

Iodomethylate of 1-methyl-6-methoxy-7-benzyloxy-3,4-dihydroisoquinoline (XII). Heating 4.05 g of (XI) and 20 g of methyl iodide under reflux for 3 hours gave a yellow crystalline precipitate. The precipitate was collected and washed several times with ether. The yield was 6.07 g (almost quantitative). The m.p. was 186—187°.

Chloromethylate of 1-methyl-6-methoxy-7-benzyloxy-3,4-dihydroisoquinoline (XIII). By Ishiwata's method [12], 5 g of the iodomethylate (XII) in 100 ml of water was shaken for 7 hours with freshly-prepared silver chloride, prepared from 5 g of silver nitrate. The silver iodide liberated was removed by filtration and washed with distilled water. The filtrate was evaporated to dryness in vacuum. A yellow crystalline substance remained. The yield was 3.45 g (97%). The m.p. was 136.5—137.5° (from a mixture of methanol and ether).

Found %: N 4.36, Cl 10.33. $C_{19}H_{22}O_2NCl$. Calculated %: N 4.21; Cl 10.68.

1,2-Dimethyl-6-methoxy-7-hydroxy-1,2,3,4-tetrahydroisoquinoline (XIV). a) Reduction of the chloromethylate in the presence of platinum oxide. 4.65 g of the chloromethylate (XIII) was dissolved in 100 ml of anhydrous alcohol and hydrogenated for 6 hours with shaking in the presence of 0.34 g of platinum oxide. A volume of 800 ml of hydrogen was absorbed. The catalyst was removed by filtration and the filtrate acidified with concentrated hydrochloric acid and vacuum distilled to dryness. The residue was treated with an aqueous solution of ammonia and the liberated base extracted with several portions of ether. The ether solution was dried with anhydrous magnesium sulfate and evaporated to a volume of 3 ml. The crystals which formed were collected and washed with ether. The yield was 0.95 g (32%). The m.p. was 148—150° (from methanol and ether).

Found %: C 69.57; H 8.51; N 6.75. $C_{12}H_{17}O_2N$. Calculated %: C 69.87; H 8.26; N 6.75.

b) Reduction of iodomethylate with zinc dust. 15 g of the iodomethylate (XII) was dissolved with stirring and heating in 375 ml of concentrated hydrochloric acid. Over a period of 2.5 hours, 56.3 g of zinc dust was added at 70—75°, and then the mixture was heated at 90° for 1.5 hours. The undissolved zinc was removed by filtration. The filtrate was washed many times with ether until the ether solution no longer became colored. (It was usually necessary to wash it 12—15 time to remove impurities. The aqueous solution was then made alkaline with aqueous ammonia (450 ml), with cooling and again extracted several times with ether. The ether solution was dried with anhydrous magnesium sulfate and the ether removed on a water bath. The residue weighed 6.77 g. It was recrystall-

ized from methanol. The yield was 3.64 g (49.6%). The m.p. was 148–150°.

2 g of base (XIV) was dissolved in a small amount of alcohol and to the solution was added an ether solution of hydrogen chloride. The precipitated 1,2-dimethyl-6-methoxy-7-hydroxy-1,2,3,4-tetrahydroisoquinoline hydrochloride was recrystallized from isopropyl alochol. The yield was 1.2 g. The m.p. was 190–192°.

Found %: N 5.69; Cl 14.66. $C_{12}H_{18}O_2NCl$. Calculated %: N 5.74; Cl 14.55.

3,4,5-Trimethoxybenzoic ester of 1,2-dimethyl-6-methoxy-7-hydroxy-1,2,3,4-tetrahydroisoquinoline (XV). 1.95 g of 1,2-dimethyl-6-methoxy-7-hydroxy-1,2,3,4-tetrahydroisoquinoline was dissolved in 15 ml of dry pyridine, 2.30 g of 3,4,5-trimethoxybenzoyl chloride added, and the mixture heated for 4 hours at 50–60°. When the mass had cooled it was treated several times with ether. The ether solution was washed with water and several times with 1 N sodium hydroxide solution and dried with anhydrous magnesium sulfate. The ether was removed and the residue (1.6 g) recrystallized twice from a mixture of methanol and ether. It formed coarse prisms. The yield was 0.56 g. The m.p. was 129–130°.

Found %: C 66.01; H 6.79; N 3.85. $C_{22}H_{27}O_6N$. Calculated %: C 65.80; H 6.78; N 3.49.

SUMMARY

1. Two comparable methods are described for preparing 3-methoxy-4-benzyloxyphenylethylamine from vanillin through ferulic acid and from vanillin through 3-methoxy-4-benzyloxybenzaldehyde. The latter route was more convenient.

2. The 3-methoxy-4-benzyloxyphenylethylamine was used to prepare several isoquinoline compounds, derivatives of isomeric salsolin: 1-methyl-6-methoxy-7-benzyloxy-3,4-dihydroisoquinoline and its iodomethylate and chloromethylate, and 1,2-dimethyl-6-methoxy-7-hydroxy-1,2,3,4-tetrahydroisoquinoline and its 3,4,5-trimethoxy - benzoic ester.

The isoquinoline compounds were sent for pharmacological study.

LITERATURE CITED

[1] M. Onda, M. Kawanishi, and M. Sasamoto; J.Pharm. Soc. Japan 76, 409 (1956); C. A. 13930[b] (1956).

[2] Organic Reactions [In Russian] 1, 316 (1948).

[3] L. Helfer, Helv. Chim. Acta 7, 950 (1924).

[4] L. V. Volkova, Diss. "Synthesis of esters of bisbenzyltetrahydroisoquinoline bases (analogs of the alkaloid curarine) " [In Russian]. M. V. Lomonosov Moscow Institute of Fine Chemical Technology (1953).

[5] D. Davidson and M. Bogert, J. Am. Chem. Soc. 57, 905 (1935).

[6] E. Spӓth, A. Orechoff, and F. Kuffner, Ber. 67, 1214 (1934).

[7] M. Moore, H. Wright, M. Vernsten, M. Freifelder, and R. Richards, J. Am. Chem. Soc. 76, 3656 (1954).

[8] F. Tiemann and N. Nagai, Ber. 11, 650 (1878).

[9] K. Brand and G. Westerburg, Arch. Pharmaz. u. Ber. Dtsch. Pharmaz. Ges. 269, 326 (1931).

[10] S. Kobayashi, Scient. Papers Inst. Phys. Chem. Res. 6, 149 (1927); Zbl. 1928, I, 1028.

[11] J. Gullard and R. Haworth, J. Chem. Soc. 1928, 581.

[12] S. Ishiwata and T. Nazaki, J. Pharm. Soc. Jap. 71, 1261 (1951); C. A. 46, 5590[a] (1952).

INVESTIGATION OF THE FUROCOUMARINS OF CULTIVATED PARSNIPS

N. P. Maksyutina and D. G. Kolesnikov

The cultivated parsnip (Pastinaca sativa L.) is a herbaceous biennial of the carrot family, which is distributed through almost the whole of Europe and everywhere in the USSR. It is cultivated   for the sake of their succulent, sweetish, aromatic roots, which are used as food.

Few chemical studies have been made of the cultivated parsnip. Work published in the literature on the parsnip is largely concerned with the carbohydrate composition of the root [1] and the essential oil of the seeds [2]. Apart from the essential oil (1.5 – 2.5%), consisting mainly of octyl butyrate [3] and free acids (butyric, propionic, and caproic [4]), the seeds were also found to contain a fatty oil [5] and two furocoumarins, namely, imperatorin and bergaptene [6]. Of the substances isolated, imperatorin and bergaptene are of medicinal importance as they have quite an active photosensitizing action and are used in some countries for the treatment of leucoderma (vitiligo) [6].

The purpose of our investigations was the isolation from cultivated parsnips of substances with a spasmolytic action. The result of these investigations is the isolation from parsnips of seven crystalline substances with varying degrees of spasmolytic activity. The main substance causing the spasmolytic action of cultivated parsnips is one with the formula $C_{12}H_8O_4$, which we called pastinatsin [7]. Pastinatsin and the six other substances accompanying it were investigated chemically. We determined the melting points, crystal forms, solubilities in the usual solvents, molecular weights, elementary compositions, presence of lactone properties, number of methoxyl groups, and the possibility of forming furandicarboxylic acid, and prepared some derivatives (alloimperatorin, the nitroderivative of bergaptene, and free phenols). The presence of lactone properties and the formation of furandicarboxylic acid by all seven substances and also the characteristic ultraviolet absorption spectra showed that these compounds were furocoumarins. The results of acid hydrolysis showed that only one substance had a side chain and the other six furocoumarins did not contain side groupings that could be eliminated by hydrolysis.

By comparing the properties of the substances obtained with known furocoumarins, we came to the conclusion that substance A was identical with imperatorin (I), substance B with bergaptene (II), substance E with isopimpinellin (III), and substance F with xanthotoxol (IV).
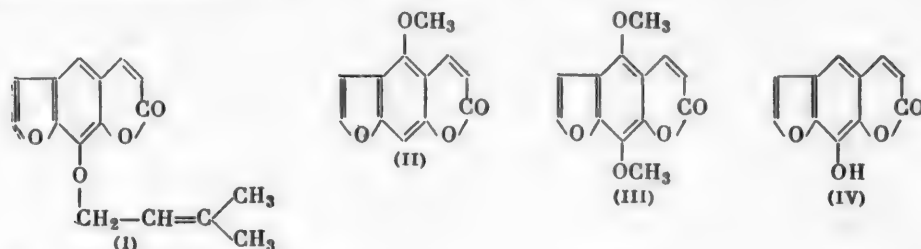
As regards the other three substances, pastinatsin, substance C, and substance G, we were unable to identify them with any known furocoumarins.

EXPERIMENTAL

Extraction of furocoumarins from parsnip seed. 10 kg of ground parsnip seed was extracted with ethyl alcohol. The alcohol was distilled from the extract completely in vacuum. The residue was diluted to 1 liter with chloroform

and a water-soluble tar precipitated by the addition of 4 liters of ligroin to the solution obtained. The precipitated red-brown tar contained hardly any furocoumarins; it was removed and the filtrate used for further separation.

Chromotographic separation of furocoumarins. The clear ligroin-chloroform solution remaining after separation of the tars was chromatographed on a column of 6 kg of aluminum oxide. The eluates were collected and each fraction analyzed for the furocoumairn content by paper chromatography and qualitative tests. The results of the chromatographic separation are given in the table.

Fraction No.	Eluting solvent	Amount of solvent (in liters)	Residue (in g)	Qualitative composition of furocoumarins
1		2.0	20.0	Oil
2		3.0	27.0	The same
3	Chloroform and ligroin (1 : 5)	3.0	76.0	The same
4		3.0	14.0	The same
5		3.0	7.0	Imperatorin and oil
6	The same (1 : 4)	4.0	8.4	Imperatorin
7		2.0	2.3	The same
8	The same (1 : 3)	3.0	3.6	Isopimpinellin
9		3.0	6.2	Bergaptene, substance C, pastinatsin, and xanthotoxol
10		3.0	10.0	Bergaptene, substance C, pastinatsin, substance G, and xanthotoxol
11	The same (1 : 2)	3.0	9.0	The same
12		3.0	5.2	The same
13		3.0	1.4	The same
14		3.0	Traces	Traces
15	The same (1 : 1)	2.0	4.6	Tar
16	Chloroform	2.0	2.1	The same
17	Chloroform and ethyl alcohol (1 : 1)	2.0	3.7	Tar and inorganic salts
18	Ethyl alcohol	2.0	2.2	The same

Isolation and Investigation of Furocoumarins

Substance A (imperatorin). Fractions 5—7 were evaporated to small volume to yield needle-like crystals with m.p. 96.5°. Recrystallization from hot benzene gave substance A in the form of dense, coarse prisms with m.p. 100—102°. Substance A dissolved very readily in chloroform, benzene, and alcohol, and very sparingly in water.

Found %: C 71.2; H 5.36. No free OCH_3 groups were present. $C_{16}H_{14}O_4$. Calculated %: C 71.10; H 5.22.

Demonstration of lactone properties of A. 0.2 g of substance A was dissolved in 10 ml of a 10% methanol solution of KOH. The yellow solution was left at room temperature for 6 hours, then diluted with 200 ml of water and the alcohol removed from the solution in vacuum. The residual solution was neutralized with HCl and extracted twice with ether. The ether solution was evaporated to small volume; substance A crystallized in an unchanged state.

Acid hydrolysis of substance A. 2.0 g of substance A was dissolved in 20 ml of acetic acid, two drops of concentrated H_2SO_4 added, and the solution left at room temperature. After 3—4 hours, a crystallize product with a slightly yellowish color began to separate. After 6 hours the crystals were collected and recrystallized from acetic

acid. After recrystallization from ether and drying, the crystals had m.p. 242—244° and were readily soluble in alkalis, and sparingly so in organic solvents and water. The yield was 1.2 g.

Found %: C 64.93; H 3.05. No free OCH$_3$ groups were found. C$_{11}$H$_6$O$_4$. Calculated %: C 64.87; H 3.09.

The phenol obtained was identical in properties and composition to xanthotoxol.

Isomerization of substance A (preparation of alloimperatorin). 2.5 g of substance A isomerized at 200—205° and a pressure of 0.01 mm in 7 minutes. When the pressure was reduced to 0.001 mm and the temperature raised to 210—215°, the isomer of substance A sublimed as bright yellow needles. After recrystallization from ether the isomer had m.p. 233°.

Found %: C 71.02; H 5.33. C$_{16}$H$_{14}$O$_4$. Calculated %: C 71.10; H 5.22.

The isomeric substance was readily soluble in alkalis to give bright yellow solutions. It was identical in properties with alloimperatorin.

Substance B (bergaptene). The eluate fractions 9—13 were combined, evaporated to small volume in vacuum, and the residue left to crystallize. After 2—3 hours crystallization was complete and the crystals were collected and dried. The total yield of crystalline product was approximately 18—20 g. The product obtained was dissolved in benzene (150 ml) by heating on a water bath. As it cooled, the benzene solution began to deposit crystals of substance B as long white needles. They were collected, dried, and recrystallized twice from hot alcohol. Substance B dissolved very readily in chloroform, with somewhat more difficulty in alcohol and benzene, and hardly at all in water. It melted at 189—191°.

Found %: C 66.71; H 3.70; OCH$_3$ 13.2. C$_{12}$H$_8$O$_4$. Calculated %: C 66.67; H 3.73; OCH$_3$ 12.6.

Demonstration of lactone properties of substance B. An alcohol solution of substance B (0.1 g in 20 ml) was divided into two portions. When water was added to one portion, there immediately began the separation of needle-like crystals which were identical in properties with substance B. To the second portion of the alcohol solution was added a solution of potassium hydroxide and then the mixture was diluted with water. In this case the initial substance B was not precipitated. When the excess alkali was neutralized and the alcohol removed by distillation, the starting material rapidly precipitated.

Preparation of nitro derivative of substance B (nitrobergaptene). 4.0 g of substance B was ground with 20 ml of acetic acid and then 100 ml of HNO$_3$ was added. The mixture was cooled and after 20 minutes it was poured into 4 liters of cold water. The precipitated product was collected, dried, and recrystallized from acetic acid. The yellow, prismatic needles of the nitro derivative became brown at 230° and melted at 256° (decomp.).

Found %: C 55.32; H 2.81. C$_{12}$H$_7$O$_6$N. Calculated %: C 55.15; H 2.79.

Oxidation of substance B with hydrogen peroxide. 0.5 g of substance B was dissolved in 40 ml of a hot 5% solution of NaOH, the solution cooled, and 22.5 ml of 3% H$_2$O$_2$ added at room temperature. The mixture was left for 20 minutes at room temperature and then heated to 80° for 6 hours. The dark-yellow solution was acidified with HCl and treated with ether. Removal of the ether from the ether extract gave 0.5 g of a crystalline mass, which sublimed at 160—170° and 0.01 mm. The sublimation yielded 0.25 g of colorless crystals which melted at 220—221° after recrystallization from ethyl acetate. The substance was readily soluble in water and alcohol, and sparingly so in ether and ethyl acetate.

Found %: C 45.98; H 2.62. C$_6$H$_4$O$_5$. Calculated %: C 46.15; H 2.58.

The substance was identical in properties to furan-2,3-dicarboxylic acid.

Substance C. The benzene mother solution, after separation of substance B, was evaporated in vacuum. The residue was dissolved in hot alcohol and left to recrystallize. On cooling, the solution first deposited crystals of substance B as needles, which were separated, and the solution heated slightly and then left for substance C to crystallize. Substance C crystallized as dense white prisms with m.p. 145—147°. It dissolved readily in chloroform, alcohol, benzene, and acetone, and more difficultly so in ether and water.

Found %: C 63.64; H 4.27; OCH$_3$ 26.2. C$_{13}$H$_{10}$O$_5$. Calculated %: C 63.40; H 4.10; OCH$_3$ 25.21.

Substance C had lactone properties and gave furan-2,3-dicarboxylic acid when oxidized with H_2O_2.

Pastinatsin. Pastinatsin crystallized from the alcohol mother liquor remaining after separation of substance C. The crystals were fine, slightly yellowish needles with m.p. 124-138°. Pastinatsin was readily soluble in chloroform, alcohol, benzene, and acetone, and more difficultly so in ether and water.

Found %: C 66.68; H 3.75; OCH_3 12.74. $C_{12}H_8O_4$. Calculated %: C 66.67; H 3.73; OCH_3 12.6.

Pastinatsin had lactone properties and gave furan-2,3-dicarboxylic acid when oxidized with H_2O_2.

Substance E (isopimpinellin). The solvent was distilled from fraction 8 of the eluate (see Table) in vacuum. On standing, the oily residue deposited a dense layer of crystals, which were collected and recrystallized several times from alcohol. Substance E crystallized as fine yellow needles with m.p. 149-151°, which grew together in a felt-like mass. The crystals dissolved readily in chloroform, benzene, and alcohol, with somewhat more difficultly in acetone, and sparingly in water.

Found %: C 63.42; H 4.10; OCH_3 26.3. $C_{13}H_{10}O_5$. Calculated %: C 63.40; H 4.10; $2OCH_3$ 25.21.

Substance E had lactone properties and gave furan-2,3-dicarboxylic acid on oxidation with H_2O_2. Substance E was identical in properties to isopimpinellin.

Substance F (xanthotoxol). The mother liquor after separation of the pastinatsin crystals was evaporated and the residue dissolved in ether. On standing, the solution deposited rhombic crystals with m.p. 240-244°. The substance dissolved readily in alkaline solutions, alcohol, and chloroform, but was difficultly soluble in water.

Found %: C 64.97; H 3.07. $C_{11}H_6O_4$. Calculated %: C 64.87; H 3.09.

Substance F had lactone properties and gave furan-2,3-dicarboxylic acid on oxidation with H_2O_2. In composition and properties, substance F was identical to xanthotoxol, whose melting point it did not depress.

Substance G. The mother liquor after separation of substance F was diluted with three volumes of ligroine. This yielded a very small amount of needle-like crystals of substance G with m.p. 140-144°.

Found %: C 66.82; H 3.81; OCH_3 12.3. $C_{12}H_8O_4$. Calculated %: C 66.67; H 3.73; OCH_3 12.6.

The compound had lactone properties and gave furan-2,3-dicarboxylic acid on oxidation with H_2O_2.

SUMMARY

1. Seven crystalline natural furocoumarins were isolated from cultivated parsnips. The substances isolated were examined chemically and a number of their derivatives prepared.

2. Four of the substances were identified with previously known natural furocoumarins: imperatorin, bergaptene, isopimpinellin, and xanthotoxol. The properties of the furocoumarin which we called pastinatsin and those of substances C and G did not correspond to any furocoumarins described previously. Apparently, we were the first to obtain these compounds.

3. The main substance causing the spasmolytic action of parsnips is pastinatsin.

LITERATURE CITED

[1] Van Urk, Pharm. weekbl. 57, 983 (1920).

[2] H. Gutzeit, Lieb. Ann. 177, 372 (1875).

[3] Haensel, Apoth. Ztg. 22, 274 (1907).

[4] Bericht von Schimmel, oct., 96 (1908).

[5] C. Wehmer, Die Pflanzenstoffe 2. (Jena, 1931) p. 894.

[6] T. O. Soine, Hamed, Abu-Shady, F. E. Di Gangi, J. Am. Pharm. Ass., Sci Ed. 45, 426 (1956).

[7] N. P. Maksyutina and D. G. Kolesnikov, Med. Prom. SSSR 6, 12 (1958).

INVESTIGATION OF ACONITE ALKALOIDS

XVI. STRUCTURE OF ELDELINE

A. D. Kuzovkov and T. F. Platonova

S. Ordzhonikidze All-Union Chemico-Pharmaceutical Scientific Research Institute

As was shown previously [1], eldeline is identical with the alkaloid deltaline. Carmack et al. [2] obtained delpheline from the latter by replacing the hydroxyl by hydrogen and hydrolyzing the acetoxy group. Since the structure of delpheline (I) was established by Cookson and Trevett [3], for elucidation of the structure of eldeline there remained the determination of the position of the hydroxyl group eliminated in the conversion to delpheline. We had reported [1] that 3 moles of $NaIO_4$ was consumed in the oxidation of demethyleneeldelidine, the product of hydrolyzing the acetoxy group in eldeline and converting the methylenedioxy group into a glycol group. Hence the conclusion was drawn that demethyleneeldelidine contains four adjacent hydroxyls. This led us to formulas (II), (III), and (IV) for eldeline, eldelidine, and demethyleneeldelidine, respectively.

However, the assumption that demethyleneeldelidine contains four adjacent hydroxyl groups was found to be incorrect: when demethyleneeldelidine was oxidized in a neutral aqueous solution, only 2 mole of $NaIO_4$ and not 3 were consumed. Apparently, when the oxidation with $NaIO_4$ was carried out without neutralization of the base, not only the glycol, but also some other groups were oxidized due to the high alkalinity of the solution (a 1% solution of demethyleneeldelidine has pH 10.3). A similar observation was made in the oxidation of delcosine with $NaIO_4$ [4].

Oxidation of demethyleneeldelidine with $NaIO_4$ led to amphoteric, uncrystallizable products which were difficult to obtain in a discrete state. On the other hand, the $NaIO_4$ oxidation of the neutral lactam corresponding to demethyleneeldelidine yielded crystalline substances. For the preparation of this lactam, eldeline was oxidized with $KMnO_4$ to oxoeldeline (the infrared spectrum contained a band at 1625 cm^{-1} of a lactam carbonyl in a six-membered ring); the latter was hydrolyzed to oxoeldelidine and the methylenedioxy group of this was cleaved with hydrochloric acid by the method used by Cookson and Trevitt for cleaving this group in oxodelpheline. The main reaction product (other reaction products will be examined at the end of the article) did not contain a methylenedioxy group or ketone groups (no absorption in the region of 1700 cm^{-1}). The formation of this substance (which we will subsequently refer to as demethylenoxoeldelidine) can best be explained by simple (unaccompanied by rearrangement) conversion of the group $-\overset{|}{C}-O-CH_2-O-\overset{|}{C}-$ into the glycol group $-C(OH)(HO)C-$. This explanation of the reaction agrees with the results presented below for the oxidation of demethylenoxoeldelidine with periodic acid, which confirms that this compound contains the grouping $-CH(OH)-\overset{|}{C}(OH)-\overset{|}{C}(OH)-CH_2-\overset{|}{C}(OCH_3)$, formed from.

$$-CH(OH)-\overset{|}{\underset{|}{C}}-\overset{|}{C}-CH_2-\overset{|}{C}(OCH_3).$$
$$OCH_2O$$
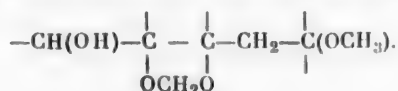
Two moles of $NaIO_4$ were consumed in the oxidation of demethylenoxoeldelidine; the reaction product was a neutral lactone whose infrared absorption spectrum did not contain OH group bands, but did contain bands at 1789, 1714, and 1640 cm^{-1}. The first of these was caused by a γ-lactone group, the second characterized the two carbonyl groups formed by cleavage of the triol, and the third was caused by the presence of the lactam carbonyl. The presence of an aldehyde group in the oxidation product was indicated by color reactions and also the fact that

oxidation of the lactone formed a lactono acid, differing in composition from the lactone by 1 oxygen atom. This acid was titrated by alkali in an aqueous solution and its infrared spectrum contained bands at 3300 (OH), 1789 (γ-lactone), 1714 (ketone or aldehyde group), and 1638 cm^{-1} (lactam).

When the lactone was dissolved in 4% NaOH, even at room temperature, the lactone ring was opened; the equivalent of alkali was bound in approximately 1 hour. Acidification of the alkaline solution and extraction with an organic solvent yielded a hydroxy acid (ν_{max} 3300, 1725, 1705, 1650, 1613 cm^{-1}), which was converted into a lactone by heating in sulfuric acid. The lactone formed was an unsaturated substance, containing an OCH$_3$ group less than the original saturated lactone. The ultraviolet spectrum of the unsaturated lactone showed absorption at 242 mμ (lg ε 3.85), characteristic of α,β-unsaturated ketones. Thus, the formation of a double bond was the result of elimination of a methoxyl in a position β to the keto group: $CO-CH-C(OCH_3) \rightarrow CO-C=C$. This instability of β-methoxy ketones under the action of acids has been observed many times in investigations of aconite alkaloids [3, 5, 6]. The infrared spectrum of the unsaturated lactone contained bands at 1756 cm^{-1} (γ-lactone), 1700 cm^{-1} (aldehyde), and a broad band at 1668 cm^{-1} (lactam and α,β-unsaturated ketone), but OH group bands were absent.
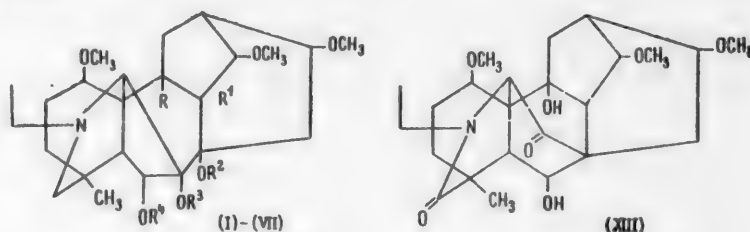
(I) R=R'=H ; R^2+ R^3=CH$_2$; R^4=H .
(II) R=H ; R'=OH ; R^2+ R^3=CH$_2$; R^4=COCH$_3$.
(III) R=H ; R'=OH ; R^2+ R^3=CH$_2$; R^4=H .
(IV) R=H ; R'=OH ; R^2=R^3=R^4=H .
(V) R=OH , R'=H ; R^2+ R^3=CH$_2$; R^4=COCH$_3$
(VI) R=OH ; R'=H ; R^2+ R^3=CH$_2$; R^4=H .
(VII) R=OH ; R'=R^2=R^3=R^4=H .
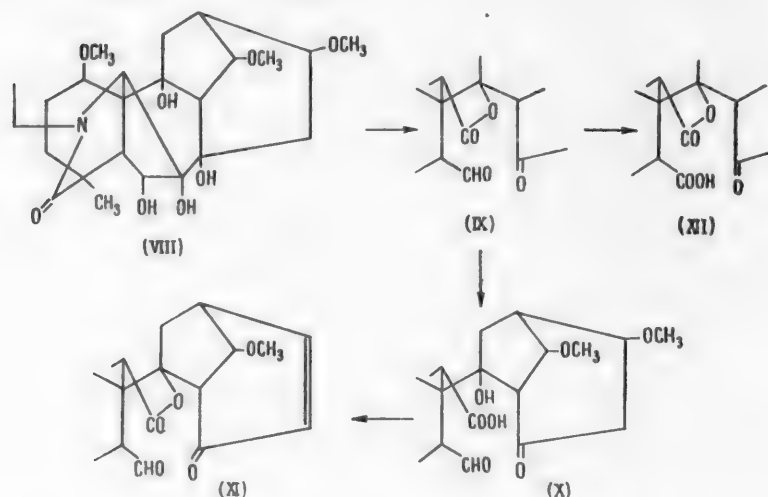
The formation of a γ-lactone in the oxidation of demethylenoxoeldelidine and the fact that eldelidine is stable to oxidation by periodic acid * quite unequivocally determines the position of the OH group in demethyl-enoxoeldelidine, which is not oxidized by periodic acid or, in other words, does not contain a 1,2,3-triol grouping.

---

* This fact, which was reported previously [1], excluded the possibility of the hydroxyl being adjacent to a secondary OH group in eldelidine.

Since this hydroxyl is eliminated by conversion of eldeline to delpheline, the data presented make it possible to represent the structure of eldeline by formula (V), eldelidine by (VI), demethyleneeldelidine by (VII), demethyl-enoxoeldelidine by (VIII), the lactone by(IX), the hydroxy acid by (X), the unsaturated lactone by (XI), and the lactono acid by (XII).

As noted above, the action of hydrochloric acid on oxoeldelidine gave other products apart from the demethylene derivative. Substance No. 1, $C_{25}H_{37}O_8N \cdot H_2O$, which was isomeric with oxoeldelidine, contained a methylenedioxy group, was not oxidized by periodic acid, and was converted into demethylenoxoeldelidine by the action of hydrochloric acid. A similar substance, isooxodelpheline, was isolated by Cookson and Trevitt [3] after treatment of oxodelpheline with hydrochloric acid in preparing the demethylene derivative from it. Isooxodelpheline contained a tertiary hydroxyl group instead of the secondary one of oxodelpheline. This led Cookson and Trevitt to the conclusion that the formation of the iso-compound involved migration of the methylenedioxy group, which was attached to two tertiary hydroxyls in oxodelpheline and to a secondary and a tertiary in the iso-compound.

Substance No. 2, $C_{24}H_{35}O_7N$, contained a keto group (1739 cm^{-1}) and could be obtained from demethylenoxo-eldelidine by heating the latter with hydrochloric acid. One mole of $NaIO_4$ was consumed in the oxidation of substance No. 2 to form an acid, $C_{24}H_{35}O_8N$ (ν_{max} 3400, 1734, 1625 cm^{-1}). A similar product was also obtained by the action of hydrochloric acid on oxodelpheline. As yet no explanation can evidently be offered for the formation of these substances.

Substance No. 3, $C_{24}H_{35}O_7N$, contained a keto group (ν_{max} 1712 cm^{-1}) and was not oxidized by $NaIO_4$. This substance was apparently obtained as a result of pinacol rearrangement. Its structure may be represented by formula (XIII), for example.

EXPERIMENTAL

Oxoeldeline. Over a period of 6 days, 18 g of powdered $KMnO_4$ and 200 ml of a 10% solution of acetic acid in acetone was added in 4 equal portions to a solution of 14 g of eldeline in 700 ml of acetone. Each portion was added when the solution lost its color. The filtrate, after removal of the MnO_2, was evaporated to dryness in vacuum and the residue dissolved in chloroform. The chloroform solution was washed twice with 5% NaOH and then with 5% H_2SO_4 until a negative reaction for alkaloids was obtained. The chloroform was evaporated and acetone added to the residue to give 5 g of oxoeldeline. A further 4 g of this substance was obtained by evaporating the mother liquor to about 20 ml and diluting with an equal volume of water. The oxoeldeline had m.p. 271—272° (from acetone).

Found %: C 61.49, 61.54; H 7.61, 7.54; N 2.70. $C_{27}H_{39}O_9N$. Calculated %: C 62.18; H 7.53; N 2.68.

Oxoeldelidine. a) A solution of 9 g of oxoeldeline in 80 ml of methyl alcohol and 15 ml of 50% KOH was boiled on a water bath for 1.5 hours. We obtained 5.4 g of oxoeldelidine with m.p. 228—230° (from acetone). $[\alpha]_D^{20}$-0.94°, (c 4.65, chloroform).

Found %: C 62.37, 62.58; H 7.86, 7.64; N 2.99. $C_{25}H_{37}O_8N$. Calculated %: C 62.61; H 7.78; N 2.92.

b) To a solution of 20 g of eldelidine in 1 liter of acetone was added 28 ml of CH_3COOH and 13 g $KMnO_4$ over a period of 20 minutes. After 1 hour the manganese dioxide was removed and the filtrate evaporated (finally in vacuum). The residue was dissolved in 20 ml of water and, on standing, the solution deposited oxoeldelidine. The yield was 9 g and the m.p. 228—230° (from a mixture of acetone and ether).

Action of HCl on oxoeldelidine. a) A solution of 5 g of oxoeldelidine in 25 ml of concentrated HCl was kept at 20° for 18 hours, then diluted with an equal volume of water, and extracted many times with chloroform. The chloroform solution was evaporated to dryness in vacuum at a bath temperature of not more than 50°. The addition of ethyl acetate to the residue yielded 1.3 g of substance No. 1 with m.p. 250° (from acetone); $[\alpha]_D^{20}$ + 4.10° (c 4.4, chloroform).

Found %: C 60.80, 61.09; H 7.94; 8.03; N 3.11; OCH_3 18.54. $C_{25}H_{37}O_8N \cdot H_2O$. Calculated % C 60.34; H 7.90; N 2.81; 3 OCH_3 18.68.

To the aqueous hydrochloric acid mother liquor was added excess concentrated NaOH solution, with cooling in ice, to salt out the demethylenoxoeldelidine (a saturated solution of ammonium sulfate could also be used for salting out). The alkaline solution was repeatedly extracted with chloroform. We obtained 1.2 g of demethylenoxo-eldelidine (VIII) with m.p. 278—280° (from acetone).

Found %: C 61.58, 61.46; H 7.87, 7.76; N 3.26, 2.94; OCH$_3$ 19.91. C$_{24}$H$_{37}$O$_8$N. Calculated %: C 61.65; H 7.97; N 2.99; 3 OCH$_3$ 19.89.

b) To a solution of 6.5 g of oxoeldelidine in 21 ml of HCl (1 : 1) was added a solution of 3 g of phloroglucinol in 70 ml of HCl (1 : 1). The mixture was heated at 70−80° for 20 minutes, the phloroglucide removed, and the filtrate evaporated to dryness in vacuum. The residue was treated repeatedly with hot chloroform (extract A), then dissolved in 10 ml of water, made strongly alkaline with 40% NaOH solution, and the solution extracted with chloroform (extract B). Evaporation of the chloroform from extract A, and the addition of ethyl acetate, yielded 2 g of substance No. 2 with m.p. 228−230° (from acetone).

Found %: C 63.51, 63.82; H 7.91, 8.09; N 3.64; OCH$_3$ 20.05. C$_{24}$H$_{35}$O$_7$N. Calculated %: C 64.13; H 7.84; N 3.11; 3 OCH$_3$ 20.70.

From extract B we isolated 2 g of demethyleneeldelidine.

c) 8 g of oxoeldelidine, 80 ml of HCl (1 : 1), and 4 g of phloroglucinol in 280 ml of HCl (1 : 1) were heated for 45 minutes at 80−90°. The experiment was then continued as described above; extract A yielded 1.1 g of substance No. 2 and extract B gave 5 g of a tarry product from which 0.6 g of demethylenoxoeldelidine was isolated by treatment with acetone. On standing, the filtrate deposited substance No. 3 (0.6 g) with m.p. 251−253° (from acetone).

Found %: C 64.45, 64.48; H 7.73, 7.93; N 3.30; OCH$_3$ 21.02. C$_{24}$H$_{35}$O$_7$N. Calculated %: C 64.13; H 7.84; N 3.11; 3 OCH$_3$ 20.70.

A solution of 0.5 g of substance No. 1 in 5 ml of concentrated HCl was kept at 20° for 18 hours. We isolated 0.2 g of substance No. 1 and 0.1 g of demethylenoxoeldelidine.

0.2 g of substance No. 1 in 10 ml of HCl (1 : 1) was heated for 1 hour at 80−90°. We obtained substance No. 2.

0.2 g of demethylenoxoeldelidine in 10 ml of HCl (1 : 1) was heated under the same conditions and yielded substance No. 2.

Oxidation of demethylenoxoeldelidine with NaIO$_4$. a) To a solution of 0.6 g of demethylenoxoeldelidine in 15 ml of water was added 0.3 g (about 1 mmole) of NaIO$_4$. The solution was left for 20 hours at 16−20°, then evaporated to dryness in vacuum at a temperature of not more than 30−50°. The dry residue was treated 3 times with anhydrous alcohol. The substance obtained after evaporation of the alcohol extract in vacuum (bath tempera-ture 30−35°) was recrystallized from a mixture of acetone and ether; we obtained 0.2 g of substance with decomp. p. 190−200°.

Found %: C 59.76, 59.55; H 7.83, 7.77; N 3.30; OCH$_3$ 19.35. C$_{24}$H$_{35}$O$_8$N. Calculated %: C 59.91; H 7.71; N 2.89; 3 OCH$_3$ 19.23.

b) To a solution of 0.6 g of demethylenoxoeldelidine in 15 ml of water was added 0.6 g (about 2 mmole) of NaIO$_4$. After the mixture had stood for about 20 hours, it deposited 0.28 g of lactone (IX) with m.p. 263−265° (from alcohol).

Evaporation of the aqueous mother solution in vacuum yielded a further 0.13 g of this substance. The lactone (IX) could also be obtained by NaIO$_4$ oxidation of the substance with m.p. 190−200°, obtained by oxidation of demethylenoxoeldelidine with 1 equivalent of NaIO$_4$.

Found %: C 61.78, 62.38; H 7.07, 7.03; N 3.37, 3.49, OCH$_3$ 19.49, 19.95. M 497. C$_{24}$H$_{35}$O$_8$N. Calculated %: C 62.19; H 7.17; N 3.02; 3 OCH$_3$ 20.07. M 463.5.

Oxidation of the aldehyde group of the lactone. Powdered KMnO$_4$ was added in portions over a period of 2 days to a solution of 1 g of lactone in 250 ml of acetone. The solvent was evaporated in vacuum, 10 ml of water added to the residue, and the solution acidified with 10% H$_2$SO$_4$ and extracted with chloroform. We obtained 0.4 g of lactono acid (XII) with m.p. 240° (with decomp.) (from acetone).

Found %: C 60.02, 59.85; H 6.87, 7.00. C$_{24}$H$_{35}$O$_9$N. Calculated %: C 60.11; H 6.93.

Preparation of unsaturated lactone (XI). a) 0.2 g of lactone (IX) was dissolved in 4 ml of 0.1 N NaOH. The greenish solution was acidified to congo with 20% H_2SO_4 solution. When the sulfuric acid solution was heated on a water bath it deposited a crystalline precipitate of the unsaturated lactone with m.p. 306—307° (from methanol).

Found %: C 64.01, 63.95; H 6.72, 6.63; N 3.30, 3.25; OCH_3 14.56, 14.69, $C_{23}H_{29}O_7N$. Calculated %: C 64.02; H 6.77; N 3.24; 2 OCH_3 14.38.

b) To 0.5 g of lactone (IX) was added 1 ml of 4% NaOH with cooling; the greenish solution was acidified with a few drops of 20% H_2SO_4, with cooling in ice, and repeatedly extracted with chloroform. We obtained 0.35 g of the hydroxy acid (X) which, after recrystallization from acetone, melted at 229° (decomp.) with rapid heating and at 208° (decomp.) with slow heating.

Found %: OCH_3 19.31. $C_{24}H_{35}O_9N$. Calculated %: 3 OCH_3 19.35.

0.1 g of hydroxy acid (X) was dissolved in 80 ml of hot water and the solution acidified with 20% H_2SO_4 and evaporated to 3—4 ml in a dish on a water bath. We obtained 0.05 g of unsaturated lactone (XI) with m.p. 304°.

Oxidation of substance No. 2 with $NaIO_4$. 0.75 g of substance No. 2 was dissolved in 5 ml of alcohol and 30 ml of water. To the solution was added 0.5 g of $NaIO_4$. After 20 hours the solution was evaporated in vacuum at a bath temperature of 20—30° to a volume of about 10 ml. The precipitate (0.5 g) was dissolved in 3 ml of 5% NH_4OH and the solution filtered and again acidified with 10% HCl. We obtained 0.5 g of acid with m.p. 295°.

Found %: C 61.62, 61.34; H 7.61, 7.79; N 3.16, 3.11; OCH_3 19.89; M 484. $C_{24}H_{35}O_9N$. Calculated %: C 61.92; H 7.57; N 3.00; 3 OCH_3 19.93; M 465.

SUMMARY

A formula was proposed for the alkaloid eldeline.

LITERATURE CITED

[1] A. D. Kuzovkov and T. F. Platonova, Zhur. Obshchei Khim. 29, 2782 (1959).*

[2] M. Carmack, J. P. Ferris, J. Harvey, I. R. L. Magat, E. W. Martin and D. W. Majo, J. Am. Chem. Soc. 80 497 (1958).

[3] R. C. Cookson and M. E. Trevett, J. Chem. Soc. 1956, 2689, 3121.

[4] L. Marion and R. Anet, Canad. J. Chem. 36, 766 (1958).

[5] O. E. Edwards, L. Marion, and K. H. Palmer, J. Org. Ch. 22, 1372 (1957).

[6] W. Schneider and H. Tausend, Naturwiss. 44, 512 (1957).

* Original Russian pagination. See C. B. translation.

CHEMICAL STUDY OF THE ALKALOIDS OF LINARIA VULGARIS MILL

G. P. Men'shikov, A. I. Ban'kovskii, and V. I. Frolova

All-Union Scientific Research Institute of Medicinal and Aromatic Plants

About sixty forms of toadflax (Linaria) grow in the USSR, but they have been studied very little up to now from the chemical point of view. There are reports in the literature that some forms of toadflax contain alkaloids. A thorough study has been made of only the one form Linaria popovii Kuprian, from whose herbage two alkaloids were isolated : peganine $C_{11}H_{12}ON_2$ [1] and linarine $C_{14}H_{16}O_2N_2$ [2].

Peganine was first isolated in 1929 from seeds of Peganum harmala (of the family Zygophyllaceae). Its structure was finally established by synthesis [3].

We studied alkaloids isolated from the herbage of Linaria vulgaris Mill. (of the family Scrophulariaceae). The total alkaloids were isolated by the dichloroethane method and the yield was 0.16 %. By ascending paper chromatography it was established that it consisted of one alkaloid with R_f 0.78 [the solvent was a mixture of butanol and CH_3COOH (86 : 14) , saturated with water].

For isolation of the alkaloid, the product was treated with alcohol, this washed out the dark tarry impurities. The residual light,crystalline precipitate was recrystallized from alcohol, from which the alkaloid separated as needles, joined in rosettes. The base obtained had the composition $C_{11}H_{12}ON_2$ and m.p. 208-210° (in vacuum). It was readily soluble in chloroform, soluble in alcohol and methanol, and difficultly soluble in ether, benzene, and water. It was optically inactive. It gave a series of crystalline salts with mineral and organic acids. The melting point of a mixture of peganine and the alkaloid investigated was not depressed.

When the alkaloid we isolated (and also peganine) was compared with linarine(a sample was kindly presented to us by S. Yu. Yunusov),it was established that the latter alkaloid also melted at 207-210° in vacuum and did not depress the melting point of peganine. The R_f values of the alkaloid investigated, peganine, and linarine also coincided.

Table 1 gives the melting points of peganine, the alkaloid investigated, and linarine,and their salts.

The data in Table 1 show that the alkaloid we isolated was identical with peganine. Comparison of the constants of linarine and peganine also indicated that they were identical.

EXPERIMENTAL

Isolation and purification of alkaloid. Ground air-dried green parts of the plant were isolated,moistened with 25 % aqueous ammonia solution and exhaustively extracted with dichloroethane. The alkaloids were completely extracted from the dichloroethane with 10 % sulfuric acid solution. The sulfuric acid extracts were filtered, made alkaline with 25% ammonia solution, and the alkaloids extracted from them with chloroform. The chloroform extract was dried with anhydrous sodium sulfate, filtered, and then the solvent removed on a water bath.

From 14 kg of plants we obtained 16 g of total alkaloids as a brownish, crystalline mass. The colored products were washed with small amounts of alcohol until a light-yellow powder was obtained,and this was recrystallized from alcohol. For elementary analysis,the alkaloid was recrystallized from benzene and alcohol and dried in vacuum at 78°. Table 2 gives data on the elementary analyses of the alkaloid investigated, peganine, and linarine.

TABLE 1

Melting Points of Alkaloids and Their Salts

	Peganine	Alkaloid from Linaria vulgaris	Linarine	
			literature data [2]	in our experiments
Base	209—210° (in vacuum)	208—210° (in vacuum)	190—191° (decomp.)	207—210° (in vacuum)
Nitrate	—	168—169 (decomp.)	169—170 (decomp.)	—
Hydrochloride	208	206—208	199—200	—
Picrate	199 (decomp.)	193—194 (decomp.)	—	—
Iodomethylate	187	186—187	185—186	—

TABLE 2

Elementary Analysis Data on Alkaloids (in %)

	C	H	N
Peganine	70.21	6.38	14.89
Alkaloid from Linaria vulgaris	70.33	6.61	14.58
	70.32	6.59	14.61
	70.20	6.64	—
Linarine (according to literature data[2])	68.90	6.54	12.01
	68.59	6.53	11.99
Linarine (in our experiments)	70.70	6.54	—
	70.48	6.72	—
Calculated for $C_{11}H_{22}ON_2$	70.21	6.38	14.89

Preparation of salts. 1. Nitrate . To an alcohol solution of the alkaloid was added concentrated HNO_3 (to an acid reaction to litmus) and ether. The nitrate crystallized as colorless needles. After one recrystallization from alcohol and ether it had m.p. 168-169° (decomp.) .

2. Hydrochloride. Into an alcohol solution of the alkaloid was passed gaseous hydrogen chloride. When ether was added, the hydrochloride crystallized as colorless needles which had m.p. 206-208° after one recrystallization from alcohol and ether .

3. Picrate. Mixing alcohol solutions of the alkaloid and picric acid yielded the picrate as yellow needles, aggregated in nodules. After three recrystallizations from alcohol the picrate had m.p. 193-194° (decomp.).

4 . Picrolonate. To an alcohol solution of the alkaloid was added an alcohol solution of picrolonic acid. On standing, the solution deposited yellow prisms of the picrolonate which had m.p. 186-187° (decomp.) after recrystallization from alcohol.

5. Oxalate . To a mixture of alcohol solutions of the alkaloid and oxalic acid was added ether. When the solution obtained was shaken, the oxalate immediately began to crystallize as colorless needles. After one recrystallization from alcohol and ether, the product had m.p. 170-172° (decomp.).

6. Iodomethylate. 0.2 g of alkaloid was dissolved in 5 ml of methanol and to the solution was added 2 ml of methyl iodide. The mixture was boiled for 5 hours. After evaporation of the solvent, to the residue was added 3 ml of a mixture of alcohol and ether (1 : 2) . The iodomethylate was recrystallized from a mixture of alcohol and acetone (1 : 2) . The m.p. was 186-187°.

SUMMARY

1. The alkaloid peganine was isolated from the green portions of Linaria vulgaris Mill.

2. Direct comparison of peganine with the previously described linarine established that the two alkaloids were identical.

LITERATURE CITED

[1] Trudy Vsesoyuznogo Nauchno-Issledovatel'skogo Instituta Lekarstvennykh i Aromaticheskikh Rastenii, 9 (1947).

[2] S. Yu. Yunusov and Z. F. Ismailov, Doklady Akad. Nauk Uzbek SSR, 11 (1956).

[3] E. Späth, F. Kuffner, and N. Platzer, Ber. 68, 699 (1935).

LETTERS TO THE EDITOR

SOME NEW DERIVATIVES OF CYCLOPROPENE

I. A. D'yakonov, M. I. Komendantov, I. Gokhmanova and R. Kostikov

Leningrad State University

In a previous communication [1] it was shown that it was possible to obtain ester (I) by reaction of diazo-acetic (ethyl) ester with diphenylacetylene in the presence of $CuSO_4$ as catalyst. The present investigation showed that the same reaction in the absence of catalyst at $120-130°$ formed ester (II). The yield was 17%. The m.p. was $77-78°$ (after chromatography on Al_2O_3 and recrystallization from ligroin).

Found %: C 81.66; H 6.23. $C_{19}H_{16}O_2$. Calculated %: C 81.79; H 6.10.

Alkaline hydrolysis of ester (II) yielded acid (III) with m.p. $210-211°$, which has been described in the literature [2, 3]. The yield was 87%.
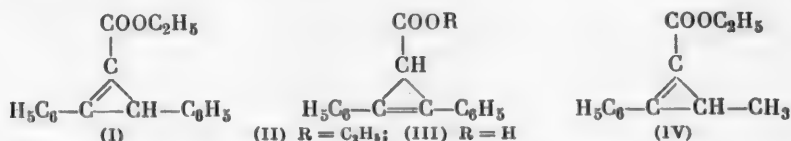
Like ester (IV), which has been described previously [4], ester (I) did not undergo alkaline hydrolysis in a nitrogen atmosphere when boiled for 10 hours with a 10% solution of CH_3ONa in CH_3OH or $(CH_3)_2CHONa$ in $(CH_3)_2$-CHOH, nor when heated for 8 hours with a 5% solution of KOH in $C_2H_4(OH)_2$ at $190°$. It is possible that the reason for the resistance to hydrolysis is steric hindrance arising in this reaction. In the readily hydrolyzable ester (II), the ester grouping is not in the plane of the ring.

Exceptional resistance to the action of alkali was also observed for ester (V), which was obtained by condensation of diazoacetic ester with octyne-4 in the presence of copper sulfate (0.8 g per mole of $N_2CHCOOC_2H_5$).

B.p. $79-80°$ (3 mm), n_D^{20} 1.45900, n_C^{20} 1.45588, n_F^{20} 1.46646, d_4^{20} 0.9253, MR_D 58.00; calcd. 57.31.
Found %: C 73.30; H 10.20; OC_2H_5 22.62. M 195.2. $C_{12}H_{20}O_2$. Calculated %: C 73.42, H 10.27; OC_2H_5 22.95. M 196.3.

Infrared spectrum: 6.10 (av., $>C=C<$), 6.25 (v. s., $>C=O$) and 9.84 $\left(\text{s.,} >\overset{-C-}{C-C}< \right)$ μ.

The observed strong displacement of the carbonyl frequency into the longwave part of the spectrum is characteristic of esters of type (V). For esters of analogous structure, (I) and (IV), this absorption band is displaced even further (6.31 and 6.30 μ, respectively) due to the presence of aromatic substituents. • The hypothesis that the

displacement of the carbonyl frequency could be caused by the presence of the polarized structure $-C^+-C=C\overset{O^-}{\underset{OC_2H_5}{\diagdown}}$

$\left(\text{instead of} -C=C-C\overset{O}{\underset{OC_2H_5}{\diagup}}\right)$, is excluded since the dipole moment found for (V) is 1.7 D and that for (I), 1.9 D.

_____

• Until (V) was prepared, these maxima were associated with the presence of phenyl groups in esters (I) and (IV).

$$COOC_2H_5$$
$$C$$
$$H_7C_3-C \!\!=\!\! CH-C_3H_7$$
(V)

$$COOC_2H_5$$
$$C$$
$$H_7C_3-C \!\!=\!\! COH-C_3H_7$$
(V A)

$$COOC_2H_5$$
$$CH$$
$$H_7C_3-C \!\!=\!\! C-COC_3H_7$$
(VI)
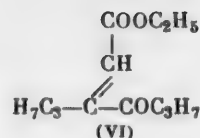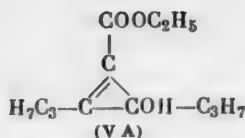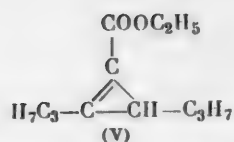
The yield of pure ester (V) was 32.6%. Crude (V) contained traces of its oxidation product (VI). When vacuum distilled in an oxygen atmosphere, (V) was completely converted into (VI). In all probability the conversion of (V) into (VI) proceeded through the formation of the intermediate structure (Va).

B.p. 97.0—98.5° (2 mm), n_D^{20} 1.4564, d_4^{20} 0.9869. Found %: C 67.35; H 9.75. $C_{12}H_{20}O_3$. Calculated %: C 67.89; H 9.50.

Infrared spectrum: 5.67 (s., >C=O), 5.81 (v. s., >C=O), 6.09 (av., >C=O <) μ.

When the reaction was carried out with a smaller amount of $CuSO_4$ (0.05—0.1 g per mole of $N_2CHCOOC_2H_5$) a mixture of (V) and the isomeric (VII) was formed. When catalyst was absent, (VII) alone was obtained. The yield was 40%.

Alkaline hydrolysis of ester (VII) gave acid (VIII).

B.p. 92—92.5° (0.5 mm), n_D^{20} 1.4625, n_C^{20} 1.4595, n_F^{20} 1.4699, MR_D 48.54; calcd. 47.96.

Found %: C 71.34; H 6.92 Equiv. 167.9. $C_{10}H_{16}O_2$. Calculated %: C 71.39; H 9.59. Equiv. 168.2.

Infrared spectrum: 5.91 (v. s. >C=O) 6.11 (s., >C=C<), 9.72 $\left(w_., \overset{-C-}{>C\!-\!C>} \right)$ μ.

Oxidation of (VIII) with $KMnO_4$ gave dibutyrylmethane (XI).

$$COOR$$
$$CH$$
$$H_7C_3-C \!\!=\!\! C-C_3H_7$$
(VII) R = C_2H_5; (VIII) R = H;

$$COOR$$
$$CH$$
$$H_9C_4-C \!\!=\!\! C-C_4H_9$$
(IX) R = C_2H_5; (X) R = H;

R—CO—CH₂—CO—R
(XI) R = n-C_3H_7;
(XII) R = n-C_4H_9.
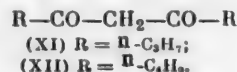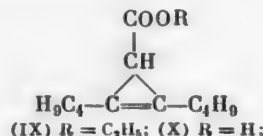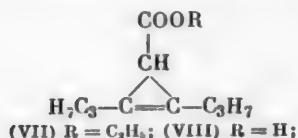
The interaction of diazoacetic ester with decyne-5 gave ester (IX). The yield was 30%.

B.p. 79—80° (0.2 mm), n_D^{20} 1.4479, n_C^{20} 1.4452, n_F^{20} 1.4542 d_4^{20} 0.8965, MR_D 66.97; calcd. 66.61.

Found %: C 74.81; H 10.83. M 219.4. Hydrol. equiv. 226.8. $C_{14}H_{24}O_2$. Calculated %: C 74.95; H 10.78. M 224.3. Hydrol. equiv. 224.3.

Infrared spectrum: 5.78 (>C=O), 6.09. (>C=C<), 9.80 $\left(\overset{-C-}{>C\!-\!C<} \right)$ μ.

Alkaline hydrolysis of (IX) gave acid (X). The yield was 89—92%.
B.p. 107.5—108° (0.2 mm), n_D^{20} 1.4612, n_C^{20} 1.4584, n_F^{20} 1.4681, d_4^{20} 0.9329, MR_D 57.76; calcd. 57.32.

Found %: C 73.33; H 10.49. Equiv. 197.6. $C_{12}H_{20}O_2$. Calculated %: C 73.43; H 10.28. Equiv. 196.3.

Infrared spectrum: 5.91 (>C=O), 6.10 (>C=C<), 9.78 $\left(\overset{-C-}{>C\!-\!C<} \right)$ μ.

Oxidation of (X) with $KMnO_4$ gave di-n-valerylmethane (XII).

LITERATURE CITED

[1] I. A. D'yakonov and M. I. Komendantov, Zhur. Obshchei Khim. 29, 1749 (1959).*

[2] R. Breslow and M. Battiste, Chem. Ind. 35, 1143 (1958).

[3] R. Breslow, R. Winter, and M. Battiste, J. Org. Ch. 24, 414 (1959).

[4] I. A. D'yakonov and M. I. Komendantov, Vestnik LGU, Ser. Fiz. i Khim. 22, 4, 166 (1956).

SYNTHESIS OF AN α-OXIDE WITH A TRIPLE BOND IN A POSITION β TO THE OXIDE RING

F. Ya. Perveev and A. V. Shchelkunov

Leningrad State University

The synthesis of α-oxides with a triple bond in a position β to the oxide ring (I) has not been achieved up to now, though their formation as intermediate products has been assumed in the preparation of some vitamins [1—3].

(I)
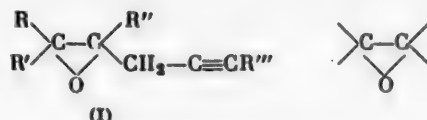
By means of the Darzan reaction, we were the first to develop a method of preparing oxides of this type. The reaction was carried out in liquid ammonia.

(II)
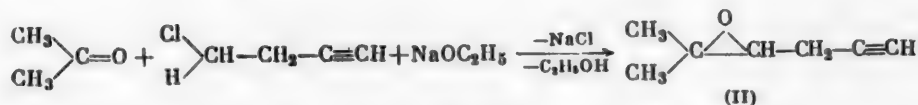
B.p. 65—67° (50 mm), n_D^{20} 1.4265, d_4^{20} 0.8680, MR_D 32.51; calcd. 32.67.

Found %: C 76.49; H 9.01. $C_7H_{10}O$. Calculated %: C 76.36; H 9.09.

(α,α'-Dimethyl-β-propynyl)-ethylene oxide (II) gave qualitative reactions characteristic of monosubstituted acetylenes and an α-oxide ring.

In addition to the oxide shown, we also isolated the product of its reaction with ammonia (III).

(III)
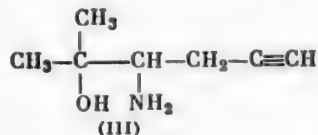
B.p. 83—84° (50 mm), n_D^{20} 1.4463, d_4^{20} 0.9014, MR_D 37.62; calcd. 37.47.

Found %: C 66.09; H 10.31; N 16.84. $C_7H_{13}ON$. Calculated %: C 66.14; H 10.24; N 16.66.

The amino alcohol gave qualitative reactions characteristic of monosubstituted acetylenes and hydroxyl and amino groups (pH about 8.5).

Work is continuing in this direction.

LITERATURE CITED

[1] L. J. Haynes, J. M. Heilbron, E. P. H. Jones, and F. Sonheimer, J. Chem. Soc. 1947, 1583.

[2] C. F. Hiskey, H. L. Slates, and N. L. Wendler, J. Org. Ch. 21, 429 (1956)

[3] T. L. Jacobs, D. Dankner, and A. P. Dankner, J. Am. Chem. Soc. 80, 864 (1958).

DISCUSSION

SYNTHESIS OF ARECOLINE

P. S. Ugryumov

Since the publication of my paper on arecoline synthesis [1], technical methods have been developed for the production of this alkaloid. N-Methyl-3-carbomethoxypiperidone-4 has become the main intermediate in this synthesis, and this compound is hydrogenated over a nickel catalyst to the labile form of N-methyl-3-carbomethoxy-4-hydroxypiperidine, which is not distilled, so as to avoid isomerization, but dehydrated to give arecaidine and arecoline. The methods developed for the hydrogenation of N-methyl-3-carbomethoxypiperidone-4 were later repeated by N. A. Preobrazhenskii et al. [2], except that they distilled the hydrogenation product of N-methy-3-carbomethoxy-4-hydroxypiperidine in vacuum and obtained considerable amounts of a stable isomer that was useless for further conversion into arecoline. My method of hydrogenating piperidone-4 into piperidol was later repeated in an American patent [3]. The most original method of synthesizing arecoline in this direction was developed by A. Dobrowsky [4].

In the paper cited [1] I also proposed the synthesis of arecoline from methylamine, formaldehyde, and acetaldehyde and this was later confirmed experimentally by C. Mannich [5]. In this connection I should also mention the synthesis of arecoline from nicotinic acid which Dr. Schubert et al., in cooperation with myself, attempted to work out in the German Democratic Republic in 1949. However, up to now, the only positive work in this promising direction is that of J. J. Panouse [6].

Simultaneously with the synthetic investigation of arecoline, I have also examined problems of cis-trans isomerism of piperidine derivatives and isomerism produced by asymmetry of the carbon atoms, the nitrogen atom, and the molecule as a whole [7].

LITERATURE CITED

[1] P. S. Ugryumov, Doklady Akad. Nauk SSSR 29, 49 (1940).

[2] N. A. Preobrazhenskii et al., Zhur. Obshchei Khim. 27 3162 (1957; 28, 968 (1958).

[3] U. S. Pat. 2776293 (January 1, 1957).

[4] A. Dobrowsky, Monatsh. 83, 443 (1952).

[5] C. Mannich, Ber. 75B, 1480 (1942).

[6] J. J. Panouse, C. r. 233, 1200 (1951).

[7] P. S. Ugryumov, Zhur. Obshchei Khim. 11, 829 (1941); 14, 987 (1944).

ARGUMENT AGAINST A SIMPLIFIED TREATMENT OF MOLECULAR SPECTRA

E. N. Prilezhaeva

Institute of Organic Chemistry, Academy of Sciences USSR

In his discussion [1], M. I. Batuev used spectroscopic data to prove that not only single, but also multiple bonds are shortened in conjugated systems. To do this he simply compared the frequencies of mutiple bonds in the oscillation spectra of ethylene and acetylene with the similar frequencies of the substituted compounds $CH_2 = CHX$ and $CH \equiv CX$. From this he concluded that there are substituents "X" which "strengthen" a multiple bond and shorten the interatomic distances (i.e. which increase its frequency), and others which "weaken" it (which reduce its frequency) and that groups $-CH = CH_2$ and $-C \equiv CH$ are of the first type.

In the first stages of the development of molecular spectroscopy, conclusions were drawn on the "weakening" or "strengthening" of multiple bonds based on a simple comparison of frequencies (see numerous papers by the French school on Raman spectra of unsaturated compounds, for example [2]. However, the so-called "characteristic" frequencies in oscillation spectra of polyatomic molecules are only arbitrarily assigned to one bond, as actually with each oscillation all the atoms oscillate and all the bonds are deformed to a greater or lesser degree. Therefore, the value of a "characteristic" frequency may change substantially from one molecule to another, due to the change in the atomic masses and elastic constants of adjacent parts of the molecule. It is this, in particular, which makes it possible to use oscillation spectra for determining the positions of bonds in molecules. However, to be able to decide on such structural details of molecules as, for example, strengthening or weakening of a given bond, strictly speaking, one should start not from the frequencies, but from the elastic constants of bonds, which cannot be known without preliminary calculation and, consequently, without an exact knowledge of the molecule's geometry. For this reason M. I. Batuev is incorrect in stating that one may readily assess the interatomic distances in polyatomic molecules from oscillation spectra. The contrary is true: for a strict analysis of spectra of such molecules, one should know their interatomic distances and valence angles.

Nonetheless, in some cases one may compare the frequencies of molecules that are similar in structure and draw conclusions from this on the changes in the elastic constants of corresponding bonds in going from one molecule to another. For this, however, one must first analyze the effect of a change in the mass of adjacent groups on the given frequency. Thus, a calculation using a simple valence-force scheme showed [3] that in the series of ethylene compounds (if they are treated as a three-body model, $CH_2 \diagdown^{CH}\diagdown X$, with the interatomic distance and elastic constant of the $C = C$ bond constant, but the substituent mass, M_X variable) the $C = C$ frequency lying in the range $1500-1700$ cm^{-1} must increase appreciably in going from ethylene ($M_X = 1$) to methylethylene ($M_X = 15$). At the same time, with a further increase in M_X from 15 to ∞, the $C = C$ frequency decreases only slightly and is found to depend little on the value of M_X over this range. It is obvious from this that the "$C = C$" frequency in various ethylene compounds can only be compared with the corresponding frequency of methylethylene and not with that of ethylene itself. The increase observed in the $C = C$ frequency in going from ethylene to methylethylene does not indicate a "strengthening" (i.e., increase in the elastic constant) of this bond or a decrease in the interatomic distance. An increase in the $C \equiv C$ valence frequencies in going from acetylene to methyl- and dimethylacetylene is also explained similarly (see Kohlrausch's monograph [4] on the general problem of the effect of the mass of an adjacent substituent on the frequency of a characteristic oscillation).

It is thus clear that a correct standard for the analysis of the change in frequencies in systems with multiple $C - C$ bonds can only be the frequency of the corresponding methyl derivative (methylethylene, methylacetylene,

etc.). It was shown by this method [3—5] that almost all substituents reduce the frequency of a multiple C—C bond, and this decrease was considerably greater in many cases than that calculated by the valence-force scheme for the mass effect. We may assume that this is due to conjugation of electrons of the double bond with unshared electrons of the substituent heteroatom (halogen, oxygen, sulfur, and nitrogen), which produces some decrease in its elastic constant (and consequently in its "multiple character"). If such a method of comparison is used for molecules containing conjugated C—C bonds, it is found that the frequencies of the multiple bonds in butadiene, vinylacetylene, diacetylene *, hexachlorobutadiene, styrene, etc. are also considerably lower than those of the corresponding methyl derivatives. However, such a comparison does not allow a strict assessment of the change in the elastic constant or the interatomic distances, as there is insufficient proof that the effect of mass is low in this series.

This letter was intended to act as a warning against a simplified treatment of molecular spectra. As was shown above, oscillation spectra do not indicate that in conjugated systems, besides appreciable shortening of single C—C bonds, there is any shortening of multiple bonds. However, other physical methods seem to indicate that the latter hypothesis is probable: thus, for example, it was recently shown electronographically [8] that the C=C distance in butadiene is 1—1.5% less than in ethylene.

This fact, however, does not contradict the concept of p-electron interaction in such systems nor that of an increase in this interaction during a chemical reaction.

LITERATURE CITED

[1] M. I. Batuev, Zhur. Obshchei Khim. 28, 3147 (1958).* *

[2] Bourguel, Bull. Soc. Chim. 53, 494 (1933).

[3] E. N. Prilezhaeva, M. V. Vol'kenshtein, and Ya. K. Syrkin, Zhur. Fiz. Khim. 14, 119 (1941); Acta phys.-chem. URSS 12, 176 (1940).

[4] K. Kohlrausch. Raman Spectra [Russian translation] (Foreign Lit. Press, Moscow, 1952).

[5] M. V. Vol'kenshtein. Structure and Physical Properties of Molecules [In Russian] (Acad. Sci. USSR Press, Moscow—Leningrad, 1955).

[6] E. Bartholomé, J. phys. Ch. B 23, 152 (1933); B 35, 442 (1938).

[7] A. V. Johnes, Pr. Roy. Soc. A 211, 285 (1952).

[8] A. Almenningen, O. Bastiansen and M. Trachtenberg, Acta Chem. Scand 12, 1220 (1958).

---

* In his article, Batuev gives for diacetylene Bartholomé's old data [6], which was corrected in a later paper [7].
* * Original Russian pagination. See C. B. translation.

SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY

ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.